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EPIDEMIOLOGY IN COUNTRY PRACTICE*

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AS I studied the long list of my illustrious predecessors who have presented the Cutter Lecture on Preventive Medicine I was truly grateful to the pious founder, that modest and yet forceful character, Dr. John Clarence Cutter, for the opportunity to visit this great country, to receive so many kindnesses from so many people and to find a truly New World opened to us on this side of the Atlantic. But what had I to offer in comparison with such eminent men? For I come to speak about very simple things, everyday happenings and elementary deductions drawn from them such as are within the scope of but a meager intellectual equipment. Yet I feel, as William Budd felt a hundred years ago, that country districts have certain advantages for the study of epidemiologic problems and that the ability of the observer is of secondary importance to his opportunities, which indeed are great. It is always my delight to quote this pioneer, whose conclusions were assailed with fierce criticism in his lifetime and who was completely forgotten until a very few years ago. I shall let him speak for himself:

> It is obvious that the formation of just opinions on the question how diseases spread may depend less on personal ability than on the opportunities for its determination which may fall to the lot of the observer.
>
> It is equally obvious that where the question at issue is that of the propagation of diseases by human intercourse, rural districts, where the population is thin and the lines of intercourse are few and easily traced, offer opportunities for its settlement which are not met with in the crowded haunts of large towns.

William Budd began his career with a term of country practice in his native village in Devonshire, where he made his memorable observations on typhoid fever.

The other pioneer whom I should like to quote is Peter Ludwig Panum, the Dane who was sent as a youngster to the Faroe Islands to investigate an epidemic of measles. Although this is also a hundred years ago there is little to add to the knowledge of the epidemiology of measles that he acquired. He wrote similarly to Budd: the isolated situation of the villages and their limited intercourse with each other made it possible in most cases to ascertain where and when the person who fell ill had been exposed to infection and to prove that the contagion could not have affected him either before or after the date stated.

Reminiscences are the privilege of the garrulous old, and I hope I shall be forgiven at this point if I am autobiographical. I recall most vividly the following incident: a gypsy woman driving a caravan into a village in the summer twilight, a sick husband in the caravan, a faulty pump at which she proceeded to wash her dirty linen, and shortly afterward my first and only serious epidemic of typhoid fever, which left me with a lasting impression of the unique advantages of the country doctor for the investigation of infectious disease. This incident showed me the ease with which an epidemic can be traced in the country and the ease with which it can be brought to an end. The handle of the Broad Street pump was removed at the urgent request of John Snow, because he believed that its clear and sparkling water contained the deadly poison of cholera. In this instance of mine, the handle was chained to the pump, where indeed it remains to this day, and there were no more primary sufferers. This was in 1910. I was twenty-five years of age and a very inexperienced assistant in a country practice, very near the one in which I have spent my life. Shortly afterward I had another memorable experience.

Now I have a friend, a very young friend — he is not yet five years of age. He is accomplished. He can play quite pleasingly on the piano. He can read and even write a little. I said to him one day, "John, you'll soon be going to school; you will enjoy that." He replied, "I'm not going to school, I know it all." That is the attitude of many young doctors entering general practice, especially if they have done a number of house jobs, and that, in those far-off days, was my attitude. I knew it all, and I got some shocks. And one of the shocks was the presence of an entirely new infectious disease — jaundice in epidemic form.

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Epidemic Hepatitis

My elderly principal, having been born, brought up and having practiced in the neighborhood, had seen several similar epidemics of jaundice. They were familiar experiences to him, and he laughed at my perplexity. However, reference to my textbooks somewhat restored my self-esteem, for the writers seemed to be, and actually were, in precisely the same state of abysmal ignorance as I was myself, and only touched on a very serious form of infectious jaundice, which they called "Weil's disease"; I pondered long and often whether this could be the same disease as that I was faced with. Others have pondered in the same way. It is a strange thought that the same agent that produced these epidemics so prevalent in country districts, and more interesting than serious, should in the late war have assumed such importance. That these epidemics have been for long prevalent in country districts is to my mind clear. So far as my own district is concerned, I have the evidence of my old principal, — no mean practitioner of his art, — the tradition of the countryside and the knowledge that seventy years ago there lived in Wensleydale a jaundice doctor who combined this useful occupation with that of a castrator.

Epidemic hepatitis as I have seen it — generally speaking requiring no treatment — is just the form of jaundice upon which a quack doctor could thrive; I suppose even he would be baffled by sufferers from stone in the common duct or cancer of the head of the pancreas. He was only doing what so many of us do — keeping his patient in a state of tranquillity while nature effected the cure. That there actually was a man who acquired this title presupposes a large number of sufferers and that most certainly of epidemic hepatitis. His remedy, by the way, was a decoction of barberry bark or the bark of the common berberis, which grows wild in the district, most likely an escape from some ancient herb garden. After 1910 I never saw epidemic jaundice until 1929, and then I saw it to some tune. In a population of 5700 there were at least 250 sufferers, and of these I myself attended 115. I do not intend to enter the clinical field beyond stating that the disease ran a mild course in the great majority of my patients. It is on the epidemiology that I wish to concentrate.

Now, those busybodies the pathologists — or that branch of them which deals with and, of course, knows all about the virus — have gravely prejudiced the issue by discovering the virus of hepatitis in the stools of sufferers from this disease and have to such an extent captured the imagination of observers that it is almost assumed that infection must be by this means and no other. He would be a bold man who now asserted that the infection

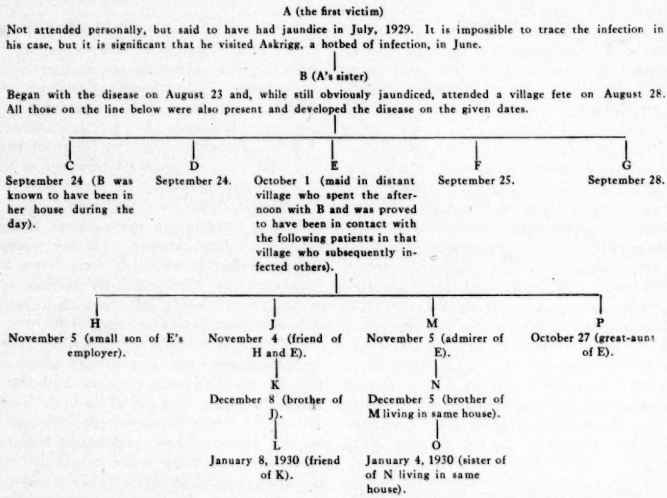
A (the first victim)
Not attended personally, but said to have had jaundice in July, 1929. It is impossible to trace the infection in his case, but it is significant that he visited Askrigg, a hotbed of infection, in June.
B (A's sister)
Began with the disease on August 23 and, while still obviously jaundiced, attended a village fete on August 28. All those on the line below were also present and developed the disease on the given dates.
C
September 24 (B was known to have been in her house during the day).
D
September 24.
E
October 1 (maid in distant village who spent the afternoon with B and was proved to have been in contact with the following patients in that village who subsequently infected others).
F
September 25.
G
September 28.
H
November 5 (small son of E's employer).
J
November 4 (friend of H and E).
K
December 8 (brother of J).
L
January 8, 1930 (friend of K).
M
November 5 (admirer of E).
N
December 5 (brother of M living in same house).
O
January 4, 1930 (sister of N living in same house).
P
October 27 (great-aunt of E).

Figure 1. *Course of Epidemic Hepatitis among Villagers Who Attended a Fete.*

could not be by the feces, but I do not want to stress that, in this and all succeeding epidemics that I have encountered, I felt justified in attributing the spread to personal contact, most likely by droplet infection. Contact sufficient to reproduce the disease was often casual, and there were no explosive outbreaks such as would have occurred from the contamination of food and water. Just the same thing has happened in poliomyelitis, and although I have not seen any reference to the discovery of virus A or B of influenza in feces — except in those of inoculated mice — I think that their presence is highly probable in this disease, and yet we shall most of us still go on believing that influenza is spread from person to person by droplet infection.

I am afraid I have repeated very often the story of a village fete depicted in Figure 1, but it gives evidence of the incubation period of about a month suggested by Booth and Okell and it is definitely my best example. Looking half way down the story one sees that five people began with the disease within a week, and I discovered that they had one experience in common: they had all been present at a fete in one of our villages on August 28. Some sufferers from the disease had therefore probably been present at the fete. After prolonged search I found that a young girl who had begun with the disease on August 23 had been at the entertainment. I had actually seen her in bed in the morning and never dreamt she could have left it. She must have eluded me with great skill throughout the afternoon, since I was there myself and never set eyes on her. She spent the afternoon with E, another young girl, and was in the house of Mrs. C., so that I think it is a fair presumption that she infected them and the other three. This young girl E, a maid in another village, infected four others. One was her employer's small son, another his friend, and another her own great-aunt. All this was reasonably clear. Of the fourth — M — there was some doubt. He was a rather pathetic little fellow of forty (since dead of a tuberculous kidney) and denied all acquaintance with this young girl. However, his sister gave him away shamelessly. "Robert not know Margaret?" said she, "Why he's very fond of her — he generally goes in at the back door in the evenings and helps her to wash up." Robert might well have said with Samson, "If ye had not plowed with my heifer, ye had not found out my riddle." A brother of Robert succumbed a month later, and in January, with poetic justice, the telltale sister. Thus, to my knowledge, one young girl determined to have what she considered her legitimate amusement, jaundice or no jaundice, and was responsible for 13 sufferers.

Figure 2 thus shows an epidemic in a family of young adults and among their friends. It shows rather clearly the monthly incubation period and suggests a short period of infectivity. I do not think one could explain this serial incidence without this assumption. I have acted on this assumption and allowed children, if they were well enough, to resume school after the fourteenth day, — well on the safe side, — with no evidence of spread of the disease. I came to the conclusion in 1930 that the incubation was about a month, the infectivity period about a week and the disease was spread by personal contact, probably by droplet infection, and I have nothing to add to these conclusions,

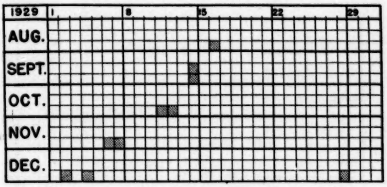

FIGURE 2. *Epidemic Hepatitis.*

since I have been fortunate enough to observe seven further — if smaller — epidemics, which have all faithfully reproduced these features.

EPIDEMIOLOGIC METHOD

Let us return for a few moments to the peculiar opportunities of the country doctor. I recall a particularly lovely evening in early summer when I climbed alone to the top of one of our noble hills. The setting sun lit up the grim pile of an ancient castle, once the prison of that unhappy queen, Mary of Scotland. Our attractive little lake seemed to lie at my feet, and one by one I made out most of our gray villages with their pall of smoke. And as I watched the evening rain creeping up the valley, with its pauses at our three stations, I had this strange thought, that there was hardly a man, woman or child in all those villages of whom I did not know even the Christian name and with whom I was not on terms of friendship. My wife and I say we know nearly all the dogs and indeed many of the cats. Now, does not this intimate knowledge of his flock put the country doctor in a superior strategic position for the study of such a subject as epidemic disease? I could say much of my patients, the Yorkshire dalesfolk; of their shrewdness and ability; of their remarkable memories; of their startling intelligence, which tempts me to deplore that in some ways education blunts the edge of intelligence; of that seemingly impenetrable crust, which is only a crust, concealing great friendliness and goodness of heart. These are just the people to help a doctor in his investigations. Matters so delicate as heredity and consanguinity have to be

approached with care, but on the whole I have found my patients co-operative and slow to take offense. Also, I cannot help knowing much about the details of their relatively simple existence. I have known the grandparents of many of my present-day patients and have been able to trace characteristics, medical and otherwise, through the generations to the present day. Today I know what markets the farmers frequent, the schools their children attend, the young people's love affairs, the festivities that take place at intervals in every village of the dale, the visits to the large towns for shopping or the yearly expedition to the Pantomime and the summer trip to the seaside. On many of these expeditions, infectious disease has been introduced into our midst, and one is rarely in doubt about the origin of any epidemic. A little help and encouragement turns the schoolmaster into an enthusiastic epidemiologist, and I have been fortunate all these years in having an ally, the headmaster of the grammar school, which serves a large area and is often responsible for the spread of epidemics. There is, moreover, stability and continuity of country practice. Most of us show but little inclination to change our habitat and retire with reluctance, knowing that our real life is then over and fearing to experience that utter loneliness which comes from a separation from our work and from our friends. Not everyone has the temperament of a Diocletian — content to throw aside the purple and grow cabbages, and, as good students of Gibbon will remember, even he lived to regret it.

You have, of course, in the United States the very best example of continuity in a practice. In 1872 George Huntington described examples of the chorea that bears his name, and it was a fact that his father, grandfather and great-grandfather had traced these sufferers through the generations and found among other things that the disease did not skip a generation.

Now a few words on technic. If one sets about to study epidemics in country practice one must have some simple technic. I carry a pocket diary, and at the bedside each sufferer is entered in the diary under the date on which the disease began — for example, March 10, 1947, Jonathan Metcalfe, aged ten, village of Aysgarth, measles and so forth. At suitable intervals these are entered on the charts (Fig. 3).

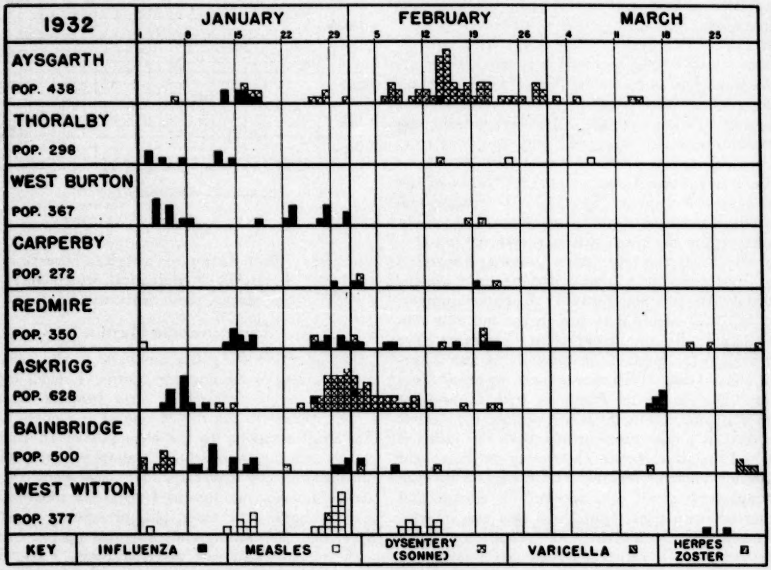

FIGURE 3. *Example of Village Epidemiologic Records (in the Actual Charts the Key Squares Are in Various Colors).*

A chart is kept of every quarter as it comes along. The names of the villages are arranged in what I consider their natural groups, the whole on graph paper. A colored square is decided on for each infectious disease, and each patient is allotted a square placed opposite the appropriate group of villages and beneath the date on which the disease began. These charts are bound in book form. The names and ages of the sufferers are written on the opposite side of the page under the particular symbol of the disease, with short notes, clinical and epidemiologic, as necessary. It is the short and only possible exposure that one is always on the lookout for; the following examples occurred during an epidemic of measles.

A man in a village remote from the prevailing epidemic exhibited the disease. Twelve days previously a friend of his had called at my surgery and, finding no one at home, had repaired to the inn conveniently situated on the other side of the road, and sat cheek by jowl with this man over their drinks. Returning to the surgery he was found to be suffering from measles. During the short visit to the inn he appeared without a reasonable doubt to have infected his companion, and the incubation period was most accurately twelve days.

A boy employed on a farm arrived at the surgery on his bicycle and announced he had "gitten mazzles" (contracted measles). This certainly was the case, and he was told to go to his mother's house and shout to her the same tidings outside the door, that she might have the living room cleared of his young brothers and sisters. He then remained in his bedroom for a fortnight. On the twelfth day after his arrival, his aunt, and only his aunt, became a victim of the disease although she had never seen the boy and had left the house the morning after his arrival. It was found that the boy's bedroom and the living room directly below, by a usual and capricious arrangement of the builder, were lighted by one long window, giving direct aerial access from one room to another. The meal table was directly below this gap and the aunt, who sat directly underneath at meals, was apparently thus infected.

Mumps pays only occasional visits and in the last large epidemic, in 1935, traversed the district with measured stride, owing to its long incubation period, and lasted a whole year. It was a long time before I had a case of the short and only possible exposure, but it arrived. Betty was a bridesmaid at a wedding outside the district on June 11. She was a rather sick little bridesmaid and was later found to have this disease. On the evening of June 26 her mother first had symptoms and a few days later showed a letter from her sister, the bride of the eleventh, stating that her symptoms had also begun on the same evening. The incubation period in the bride was definitely fifteen days. Later, I had several similar cases and the period was never less than fifteen days and never longer than seventeen or eighteen.

Influenza

At this point I think we should enter on the subject of influenza, the most important of our epidemic visitants. Influenza, more than any other disease, transforms the busy but orderly existence of the country doctor into a nightmare. To visit fifty houses as I have done in a country district and see three times that number of patients is no small feat in the space of a working day, however long. Some of these have to be visited a second time late at night and there are always visits to our *malades imaginaires*, who dread that they will be neglected in such a strenuous period. In the 1937 influenza epidemic the ferocity lasted under a month as it spread quickly from village to village, owing, I believe, to the improved methods of transport.

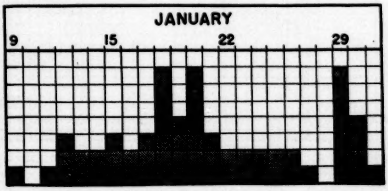

Figure 4. *Influenza.*

Lately, it has been the policy of the education authorities to close the small schools and concentrate on those in the larger villages. This may be good in the cause of education, but it adds substantially to the spread of infection. It gives us visits to isolated farms that might otherwise have escaped and many walks in the midst of strenuous days over sodden fields, not at all acceptable.

Figure 4 shows part of an epidemic in 1935. A schoolmistress returning from a Christmas visit to her parents in Scarborough, feeling far from well, attended her school on the first day of opening. She attended a brief morning session and then was quite unable to continue. In this session she was responsible for 78 victims among her charges and their families. I was not aware of this until I studied my charts later, and the worthy lady is probably not aware of it to this day. It is quite definite that this village, which was the only one to suffer severely in 1935, almost escaped in 1937, suggesting some measure of immunity in a village population. In 1946 I had the privilege and pleasure of a visit from that great Australian scientist, Professor Frank Burnet. He agreed with me on this point, and later we were able to prove from my charts that in a

village community there was a considerable degree of immunity to influenza for four years but that this declined and faded altogether in seven. I think the help I got from Burnet on this occasion illustrates what I have often said: that it is the role of the country doctor to collect facts from which others more skilled can draw conclusions.

Influenza appeared in Wensleydale in 1943, imported by a schoolmistress who had spent the half-

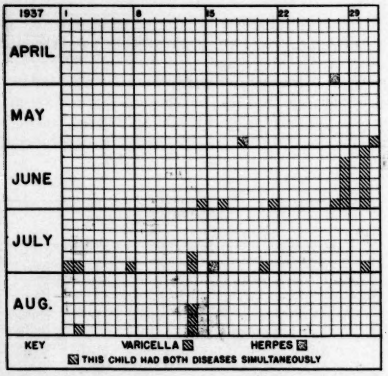

FIGURE 5. *Chicken Pox and Shingles. I.*

term holiday in Manchester. I saw several girls in this school suddenly stricken with what was undoubtedly clinical influenza in the first week of November when there was no sign of the presence of an epidemic in the country at large according to the weekly records of influenza deaths. By the end of the year these had risen to 1300 per week.

CHICKEN POX AND SHINGLES

On April 27, 1937, a young married woman exhibited the initial symptoms of supraorbital herpes. On May 18 her baby daughter developed herpes zoster in the lumbar region and widespread chicken pox, a fairly rare combination (Fig. 5). On May 31, a little girl much attached to the baby next developed the disease, but returning to school one week after falling ill, I believe, also infected this one, explaining why the entry comes out of its turn. The epidemic spread to the sister village and claimed another victim from herpes zoster. This patient lived at a farm really in the wilds, and the only possible infector was a small girl who was taken there by her mother three days before she developed a rash, suggesting that she was infectious at the time. This child also added to one's knowledge later, in that she again developed chicken pox in 1945, the only occasion in which I have attended the same patient with this disease twice.

On May 6, 1937, a young married woman developed shingles, and on the following day, a young farmer in a village four miles distant. They had an experience in common, having attended a sale in the latter's village a fortnight before and having tea at the farmer's house, his wife being a great friend of the young married woman. Infection for both appears to have been acquired at one or other of these entertainments, although in this case I was unable to trace the culprit. The male sufferer was present on the day of national rejoicing, May 12, the Coronation of King George VI, at the local junketings, which took the form of the usual tea and sport, and his victims are shown in Figure 6. The grandfather of one of these later developed shingles. I take it that the close connection between the two diseases is now firmly established, but it has been interesting on many occasions to find cases of this association, if only to show the advantages of country practice.

In the months June to October, 1940, we also had the two diseases and during the same period five sufferers from Bell's palsy. Bell's palsy has been a very rare disease to me. Actually, in thirty years of practice I had never seen a single case, and naturally 5 sufferers in a short period set me thinking. The presence of shingles and chicken pox was significant, although there appeared to be no direct connection between them and the sufferers from facial paralysis. Professor J. F.

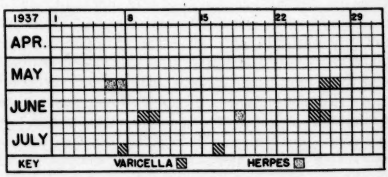

FIGURE 6. *Chicken Pox and Shingles. II.*

Bedson, of the London Hospital, most kindly undertook complement-fixation tests on the serum of three of these, but only one was positive for the virus of herpes and varicella. Thinking about this afterward, I do not consider that one would have got valuable information from these tests, except for negative reactions, for most people have had one or other disease and would presumably give positive serum results. One of the negative reactors gave us far more information by developing a most severe attack of chicken pox within the year, showing I believe, conclusively that the facial paralysis was not due to the virus. I am inclined to

believe that these sufferers were infected by some virus allied to poliomyelitis of which they were the only efflorescent examples. Later I did have a patient suffering from facial paralysis who had unmistakable herpes vesicles in his auditory meatus. In the autumn of 1947, when we also had our first experience of a poliomyelitis epidemic, one little boy developed facial paralysis with no further extension. All these patients completely recovered.

Frequency of Infectious Disease

That the charting of epidemic disease in country practice is a formidable task may be gathered from the fact that in fifteen years and three months, 4855 cases of infectious disease have been recorded (Table 1). Influenza tops the list, followed by the diarrheal diseases — often Sonne dysentery. At the bottom, thank God, comes diphtheria.

It was recently pointed out by a colleague to whom I was showing this list that perhaps teaching bodies did not realize how few of these diseases, which loom large in a general practitioner's work, are even seen by the student in his ordinary course. This seems to suggest that facilities should be given him to visit patients in their own homes so that he does not see sufferers from these diseases for the first time when he takes up practice on his own account. Furthermore, I believe from the human point of view it would be a corrective to hospital outpatients — that varied collection of interesting cases — for a student to go alone into a patient's house and find out that his life is to be spent attending to men, women and children — not cases — and also to see at first hand under what conditions they live.

Erythema Nodosum

Erythema nodosum is not a common disease in any experience and many years ago I began charting sufferers, thinking the complaint had many points in common with the exanthemas. Now the record is there so that I can follow up the connection with tuberculosis. To my sorrow in 1 case in the spring of 1946, the connection was only too obvious. A little girl of eight — the idol of her family — having just recovered from this disease, died within two days from tuberculous meningitis.

Prevention of Diphtheria

I think I should say a little about diphtheria prophylaxis. In my time in Wensleydale diphtheria has rarely appeared, but when it comes it kills, and consequently protective inoculation has now for many years been an especial care. Bearing in mind that in inoculated children added protection is acquired by subsequent actual experience of the organism, I had a little doubt whether it was possible to produce permanent immunity in a child population in which this experience was largely lacking. Dudley showed in his inoculated boys at Greenwich Hospital School that there was a temporary rise in the carrier rate, but in Hamilton, Ontario, after many years of a high percentage of inoculations, carriers virtually disappeared, suggesting that the germ had been banished from the city. That is all to the good if one remains in Hamilton, but if one becomes a Canadian soldier and is drafted to a camp in England, it is possible that one's immunity may be low and if exposed to diphtheria, one may develop diphtheria, and that is precisely what did happen.

Table 1. *Cases of Epidemic Disease.*

Disease	No. of Cases
Influenza	1112
Diarrhea and vomiting	1018
Measles	510
Febrile catarrh	407
Chicken pox	318
Whooping cough	295
Tonsillitis	289
Mumps	233
German measles	175
Herpes zoster	140
Hepatitis	122
Scarlet fever	117
Lobar pneumonia	41
Glandular fever	41
Bornholm disease	25
Diphtheria	12
Total	4855
Erythema nodosum	12

Bearing all this in mind, it was with some trepidation that I undertook a Schick-testing campaign some years ago. The numbers, I realize, are small, but this would be the experience of anyone undertaking such a campaign in a country practice. I tested in all 306 inoculated children, some two years and some five years after the inoculation. I found 36 reactors — that is, 11.76 per cent. Omitting the control and using only the toxin, reading at the end of the week even slight redness as positive, it is very probable that some pseudo-reactions were included. Therefore, the total of only 36 reactors in these children was not discouraging.

Bornholm Disease

Let me give you a personal experience of a somewhat rare infectious disease. When I have touched so lightly on the common infectious diseases I feel I must quote:

> Who goes gleaning
> Hedge-side chance blades, while full sheaved
> Stand cornfields by him.

To meet with one illness to which formal diagnosis cannot be given is no rare experience, but to be faced with a series of 7 cases of what was apparently an undescribed infectious disease was the lot of my partner, the late Dr. Dean Dunbar, and myself in the summer of 1933. I should like to emphasize the atmosphere of utter helplessness that

prevailed before a diagnosis was forthcoming, believing that a like experience might be the fate of other general practitioners.

In the early morning of a bright July day I was roused from my bed by a young farmer, thoroughly alarmed, who asked if I would come to one of his small boys who had been taken seriously ill. This boy, aged two and a half years, had been quite well and lively while being dressed but then was suddenly attacked with pain in the upper part of the abdomen, sweated profusely and was thought by his mother to have had a fit. When I saw him the pain was not so acute, but he was deadly pale, looked limp and ill, and was taking short shallow breaths, which were obviously causing him discomfort. At this stage his temperature was 98°F. Later in the morning my partner saw him with a return of the acute pain and suggested that there was a painful spasm of the respiratory muscles, probably of the diaphragm — a very acute clinical observation. We saw him together at 3 o'clock, and again the picture was changed. His face was flushed, his temperature was 101°F., and his respirations were definitely 60 to the minute. At this point we felt on firmer ground and believed that we were justified in suggesting to the parents that the child was beginning with acute pneumonia although physical signs of this disease were entirely absent. I still think, and believe you will agree, that this was a reasonable suggestion. In the evening the patient seemed better, to add to our difficulties if at the same time to bring us peace of mind. His temperature now was only 100°F., he seemed to have little respiratory distress, and he had no pain. The next morning — really, we were dealing with a strange disorder — the little rascal, standing on the window sill and thumping on the pane, greeted me smilingly, but I thought derisively, as I walked up the garden path. I examined him carefully and could find nothing to account for the happenings of the previous day; I told his mother that I had no idea what had been the matter with her boy but that his troubles were now over and that she should worry no more. This was an extremely rash remark, as I was to learn later, for on the next day I found the boy very much as he was on the first day of his illness, and he had several hours of distressing symptoms with the addition of pain in his back, which prevented him from raising himself from the bed. On the next day his evening temperature was 99.8°F., but thereafter he completely recovered. The family consisted of father, mother and three little boys in addition to the first victim, and the boon companions of the boys were three little girls who lived on the other side of the main road. Two of these were bending over the little sufferer's couch with interest and solicitude on the very first morning of the illness. I told the mother that these young women were better off in their own home until we decided what was the matter with her own child and packed them off, little thinking that the damage was already done. To cut a long story short, two of the brothers were attacked on the second and third days respectively of the first boy's illness, and the two little girls on the fourth day. Four days after his boy's complete recovery the father contracted the disease.

We were therefore dealing with an infectious disease quite unknown to us, in which our textbooks gave us no assistance and two problems presented themselves for solution, Where did this strange disease come from, and could we give it a name? The first was partially answered immediately. Four days before the appearance of the illness in the first child, 2 children were brought from the York neighborhood and spent a day on the farm. I was told that one, a little girl, spent it sobbing with pain doubled up on the sofa, and although I did not see her I have no doubt that she was the infecting party. The second problem was more difficult but was eventually solved completely. I had the good fortune the previous year to be in correspondence with Dr. Ejnar Sylvest, a general practitioner of Copenhagen, on the subject of epidemic jaundice, and he very naturally sent me articles on a condition he called "myositis epidemica" or "Bornholm disease." I was unable to read his article in Danish, but his references to epidemic pleurodynia, epidemic pleurisy and above all epidemic diaphragmatic spasm made me suspect that I was on the right track. Finally a copy of his paper submitted to the International Office of Hygiene settled the matter without a shadow of a doubt. I have had further experience with this disease and have seen in all 28 patients. Three points in diagnosis I should like to stress are the greatly increased respiratory rate, whether the pain is thoracic or abdominal; the almost invariable absence of vomiting; and the rarity and lack of prominence of cough.

This, then, is Bornholm disease, epidemic myalgia or as it is called in America, "the devil's grip," a disease of alarming symptoms but with no death rate whose only danger is that it may and has indeed come under the care of the surgeon through lack of diagnosis.

Country Beliefs

I wonder if a few words on the usefulness of the beliefs of the countryside would interest you in the way they interest me. I recall the story of a saucy little milkmaid who declared to her companion, in the pride of her youthful beauty, "I shall never get smallpox, I shall never have an ugly pock

marked face; I've had cow pox and girls who have had cow pox never catch smallpox." Jenner overheard this conversation and consulted his old chief, the great John Hunter, whose advice not to accept theories or jump to conclusions led to one of the basic discoveries in medicine. William Withering's old country woman selling her dropsy cure — country minds work on simple lines — had no doubt that it was a dropsy cure, and it is still a dropsy cure after the lapse of two centuries. My own district two or three generations ago cherished a dropsy cure — "pellitory of the wall." I have seen it growing in the neighborhood of an ancient castle, at Fountains Abbey, our best preserved Cistercian Monastery, and in New College Lane at Oxford, and I believe that in both it is an escape from a medieval herb garden. It is said to have been brought from the East at the time of the Crusades. In 1 case, an elderly colleague tells me, the diuresis it produced was so alarming he was called in to stop it. I must record that the link between chicken pox and shingles was accepted quite naturally by our country folk long before it became a commonplace in the textbooks of medicine.

* * *

I do hope I have been able to pass on to you a little of the atmosphere of a busy country practice in England, and as I speak from thirty-seven years' personal experience, it is a full and happy life. It may, of course, be a mere repetition of irksome tasks, but this is probably the fault of the practitioner who, like Bunyan's man with the muck rake "rakes to himself the straws and sticks and dust of the floor and can look no way but downward regardless of the crown which is being held above his head." I finish with a quotation from a letter of T. H. Huxley, the advice in which is so hard to follow: —

> Sit down before fact as a little child: be prepared to give up every preconceived notion: follow humbly and blindly wherever nature leads, or you shall learn nothing.

RADIOACTIVITY AND URINARY-TRACT CALCULI

DAVID S. CRISTOL, M.D.,* ALBERT E. BOTHE, M.D.,† AND PAUL W. GROTZINGER, M.D.‡

PHILADELPHIA

AN interesting observation promises to open other avenues of approach in the methods for investigating the formation of urinary-tract calculi.

A patient who proved to have a vesical calculus as well as multiple prostatic calculi recently came under our care. In the course of the physical examination he was also found to be suffering from polycythemia vera. In an effort to bring the blood hematocrit within normal limits prior to surgery, it was decided to subject the patient to radioactive phosphorus therapy and thereafter to observe any changes in the size and configuration of the calculi. In preparation for surgery, two doses of radioactive phosphorus were given orally. The first dose contained 6 millicuries, and the second, administered five months later, 10 millicuries. Periodically during the seven-month period before operation, the calculus was observed radiographically and cystoscopically and appeared to grow larger. The bacterial and chemical constituents of the urine were also repeatedly examined both before and during the course of therapy. Blood counts were made at regular intervals, and when the hematocrit appeared optimal, one of us (D. S. C.) performed a suprapubic removal of the vesical calculus, together with a revision of the vesical neck. At the time of surgery, as many of the prostatic calculi as could be dislodged from their position adjacent to the prostatic capsule were also removed.

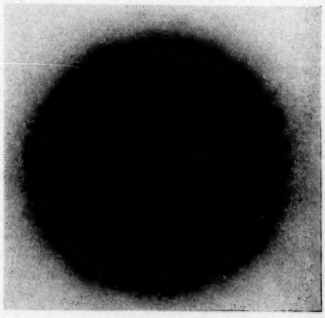

FIGURE 1. *Autoradiograph of Intact Vesical Calculus (Twenty-Four-Hour Exposure).*

These calculi were removed on the sixty-first day after the second oral dose of radioactive phosphorus. Immediately afterward they were bathed in water

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for forty-eight hours to remove the residual dried radioactive urine. Then they were placed before a Geiger counter,* and the degree of radioactivity

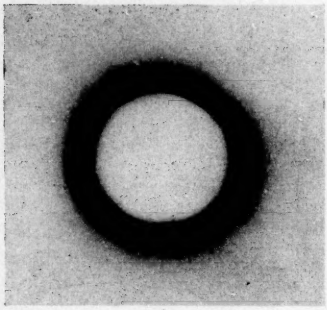

FIGURE 2. *Autoradiograph of Divided Radioactive Vesical Calculus (Twenty-Four-Hour Exposure).*
Intense area of blackening at the periphery represents deposited radioactive phosphorus.

recorded. The vesical calculus proved to be markedly radioactive. The prostatic calculi, which were not in contact with the urine and also were

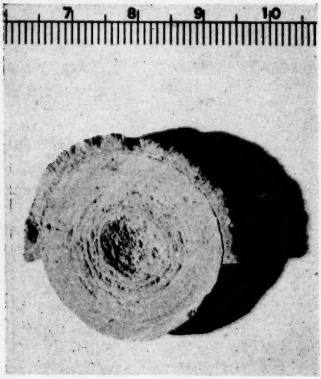

FIGURE 3. *The Divided Vesical Calculus, with a Portion of the Radioactive Lamina Removed.*

presumably not enlarging during the period of phosphorus therapy, were not radioactive. A count of 2000 per minute at a distance of 10 cm. from the window of the Geiger tube was recorded from the vesical calculus. The cosmic background count was 30 per minute. Autoradiographs were then made using four-hour and twenty-four-hour exposures of the intact vesical calculus and of the divided vesical calculus. A blackening of the film of the intact stone (Fig. 1) was obtained, with a rather hazy border that was due to the fact that the stone was somewhat semicircular in shape and that there was some scattering of the beta rays at the margin. The stone was then cut in half in its long dimension, and the flat surface placed on a film first for four hours and then for twenty-four hours as before. A ring-like area of blackening was obtained, with a

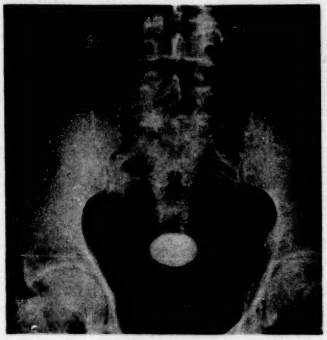

FIGURE 4. *Roentgenogram before Operation.*

somewhat hazy border. An intense area of blackening, which represented deposited radioactive phosphorus, could be seen (Fig. 2) at the outermost periphery. No radioactive phosphorus was deposited in the central portion. Thus, one has a true picture of the radioactive phosphorus in the stone and an estimate of the increase in the size of the stone during the time when the patient was receiving the drug. Figure 3 shows the divided stone, with a corresponding radioactive lamina chipped off from the lower half. Figure 4 reveals the flat plate, including the renal, ureteral and vesical areas before surgery. Further details are presented below.

CASE REPORT

A. S., a 56-year-old man, was first seen in December, 1946, complaining of marked diurnal and nocturnal urinary frequency, dysuria and intermittency of urination that had progressed over a period of approximately 2 years. During the previous 4 months, he had also suffered numerous hot flushes, frontal headaches and periodic episodes of vertigo.

The past history was noncontributory except for the fact that a physician had treated him for 6 months as a suspected case of pulmonary tuberculosis 30 years before and had estab-

*Dr. John H. Freed, of the University of Pennsylvania Radiology Department, performed the radioactivity measurements.

lished a diagnosis of polycythemia vera within the previous 3 months. The patient had been bled on several occasions, with temporary relief from the symptoms.

Physical examination gave negative results except for dusky complexion, coronal hypospadias and a moderately firm and enlarged prostate with numerous crepitant areas.

The blood pressure in both arms was 160/100. Examination of the urine revealed a moderate trace of albumin, and the sediment was loaded with erythrocytes and leukocytes. A gram stain disclosed numerous gram-positive cocci and diplococci.

An excretory urogram demonstrated a vesical calculus, numerous prostatic calculi and an essentially normal-appearing upper urinary tract.

Cystoscopy revealed 100 cc. of residual urine, minimal trabeculation, a yellow, smooth, egg-shaped calculus measuring approximately 4 cm. in length and 3 cm. in its widest diameter, a moderate degree of trilobar intraurethral prostatic hyperplasia, numerous dilated prostatic ducts and subacute cystitis over the trigone.

After a blood count had been made, the patient was given 6 millicuries of radioactive phosphorus orally on January 9, 1947. The urine, as well as the blood, was repeatedly examined. The vesical calculus was also repeatedly observed both radiographically and cystoscopically. On May 10 radioactive phosphorus in a dose of 10 millicuries was given orally.

The hematocrit became normal, and the patient was hospitalized on July 8. A roentgenogram of the chest was normal. The urea, sugar, calcium, phosphorus, proteins and alkaline and acid phosphates were all within normal limits. The blood serologic findings were negative. On July 11, under spinal anesthesia and through a suprapubic incision, the bladder was opened and the vesical calculus as well as some prostatic tissue containing calculi was removed. The pathologist reported that the removed prostatic tissue represented benign prostatic hyperplasia. The patient made an uneventful recovery and left the hospital free from urinary symptoms 3 weeks after operation.

A follow-up re-examination 3 months later revealed the urinary tract to be entirely within normal limits except for the presence of some residual prostatic calculi.

Discussion

In addition to the dramatic and graphic representation of stone formation, the employment of the radioactive element may prove to have many worthwhile uses in the study of urinary-tract-calculus formation. This method might serve as a check on various proposed methods of preventing additional stone formation. It gives an opportunity for one to observe, for example, the effect of an acid ash diet on the formation of alkaline stone. It also suggests the study of the effect of radioactive materials on associated urinary-tract infections. The possible effects of residual radioactivity in calculi on the containing tissues are also under investigation.

This is apparently the first recorded case of removal of a radioactive calculus.

Medical Tower Building

PREMEDICATION AND ANESTHESIA IN OBSTETRICS*

Current Practices at the Boston Lying-in Hospital

Bert B. Hershenson, M.D.†

BOSTON

THE first recorded obstetric operation under anesthesia in the Americas was performed by Dr. Walter Channing on May 5, 1847, at the Boston Lying-in Hospital. He wrote of his book, which was published in 1848[1] and which has become a classic, that "it treats of a noble subject, the remedy of pain" in childbirth. Today, a century later, this subject is still well deserving of consideration.

At the Boston Lying-in Hospital, there has been an evolution through various developmental phases of the subject. The keynote has always been the practice of safe relief of pain, permitting the obstetrician to carry on a conservative policy in the conduct of labor. All the known regional and inhalational anesthetic agents and technics have been employed, and all routes of the body have been utilized for the introduction of amnesic and analgesic drugs. At one time or another, Simpson's and Channing's methods of ether inhalation, John Snow's chloroform *à la reine*, intermittent nitrous oxide through long hours of vigil, twilight sleep and most of the pharmacologic agents known for their effects on the central nervous system have been administered.

Out of this experience certain facts appear significant. First and most important is the obstetric team and the environment under which it functions.[2] The greatest emphasis should be placed on the knowledge, experience, skill, judgment, attention and mutual professional confidence of the members of the obstetric team rather than on the agent or technic employed. Secondly, the complete individualization of selection of agents, dosage and routes of administration in the able hands of a well trained team of obstetrician and anesthesiologist is the only true path to safety. Thirdly, the ideal agent or combination of agents is not available to meet all the requirements necessary for safe, controllable and effective obstetric amnesia, analgesia and anesthesia. Finally, we have been impressed with the fact that our most successful methods have included the use of scopolamine.[3] Its advantages and disadvantages for the obstetric patient have been dealt with elsewhere.[2]

We are of the opinion that misuse of analgesic drugs in obstetrics is more productive of ill effects

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†Director of anesthesia, Boston Lying-in Hospital.

upon both mother and baby than properly administered inhalational anesthetic agents. Judicious selection and skillful administration of inhalation anesthetic agents are most successful for the termination of labor. Among some of the advantages of inhalation anesthesia are the rapidity of exchange of agent via the lungs, short induction and recovery periods, predictable and controllable depth and duration of anesthesia, retrievableness of the agent without residual injury, wide margin of safety, lack of extra load on the detoxifying mechanisms of the body and permissibility of employment of highly oxygenated atmospheres.

We employ regional and inhalational anesthetic procedures. The selection of agent and technic is based on many factors, some of the more important of which are physical status of the patient, the gestational age and condition of the fetus, the degree of muscle relaxation necessary to complete a given obstetric procedure, the duration and depth of narcosis required, the action of the agents selected and their influence on the conduct of labor and the skill and experience of the obstetrician and anesthetist.

For the purposes of guiding the resident and house staff in the selection of premedication and anesthetic procedures the outline presented below has been devised.

Uncomplicated Vaginal Delivery

Early in labor following the admission enema, the patient receives 0.1 gm. of seconal, usually by mouth, for the purposes of determining sensitivity to barbiturates and to provide some psychic sedation. If no untoward reaction exists she receives 0.1 gm. of seconal along with 0.1 gm. of sodium amytal at the end of an hour by mouth or rectum. If the latter route is used the ends of the capsules are perforated before administration. At that time 0.6 mg. of scopolamine hydrobromide is administered intramuscularly. The total dosage of barbiturates during labor is limited to 0.4 gm.

As labor progresses and becomes more active so that the patient complains of painful contractions of the uterus, intramuscular injections of scopolamine and apomorphine of 0.6 mg. each are given, followed in an hour by an intramuscular injection of 0.4 mg. of scopolamine and 1.2 mg. of apomorphine. The latter dosage combination of scopolamine-apomorphine is administered intramuscularly every two hours until the patient is ready for delivery. In the event that the patient shows muscular overactivity or agitation (scopolamine reaction), additional doses of 0.6 to 1.2 mg. of apomorphine are administered intramuscularly and may be repeated at intervals of fifteen minutes until the desired therapeutic response is reached. This is rarely more than two doses.

The delivery is completed under an inhalational procedure. A clear, unobstructed airway must be maintained constantly. Any cause inhibiting normal thoracic excursions must be eliminated. Employment of highly oxygenated atmospheres is encouraged, until the delivery of the fetus is completed and the cord is clamped. At the completion of anesthesia and delivery, the nurse is instructed to turn the patient on her side to drain any secretions; at the same time the patient's head is slightly extended. An unconscious patient constantly demands careful and intelligent supervision and protection.

Special Problems

Respiratory Complications

For patients with active respiratory infections, such as upper-respiratory-tract infections with temperature or cough, premedication consists of the measures outlined above for the uncomplicated case, but the barbiturates are reduced to half the dosage outlined, or less. Delivery is completed under the plan of premedication or supplemented with a regional block, usually low spinal analgesia. The spinal analgesia is administered by a member of the resident staff or under the supervision of the anesthesiologist.

For patients with asthma the barbiturates are reduced to a minimal dosage range, not exceeding 0.03 to 0.2 gm. of seconal. Scopolamine and apomorphine are administered as outlined above. The delivery is completed under inhalation anesthesia, ether being employed as the agent of choice. A skin test with the drugs and anesthetic agents before administration is given to any patient suspected of having asthma or of being allergic.

Patients with previous thoracic operative procedures or with active tuberculosis are treated as for active respiratory infections.

Cardiovascular (Circulatory) Complications

Both premedication and anesthesia are individualized for patients with Class IA cardiac disease (unfavorable cardiac cases).

For those with Class I cardiac disease (favorable cardiac cases), medication consists of administration, intramuscularly, of 100 mg. of demerol when the patient is in active labor and thereafter of 50 to 100 mg. of demerol every three or four hours. Inhalation anesthesia is employed for termination of the labor. After delivery the patient receives oxygen-enriched atmospheres as indicated.

Patients with Class II and III cardiac disease (functional) are treated like those with uncomplicated vaginal delivery, untoward manifestations being watched for.

Genitourinary Complications

If moderate to mild impairment of renal function exists the dosages of the drugs used for premedication are reduced to one half. The delivery is completed under inhalation anesthesia.

If more advanced renal-function impairment exists the drugs for premedication are omitted, or reduced to one fourth the usual dosages. The delivery is completed under a regional analgesic procedure, and the patient is provided with oxygen-enriched atmospheres.

Gastrointestinal Complications

If a patient has had food or fluid within six hours of hospital admission, she is considered as presenting the complication of a "full stomach." It must always be remembered that fluid or food in the stomach is compatible with life, but in the lungs means death. If delivery is imminent the patient's stomach is washed out, and to make certain that the procedure is successful she receives but half the usual dosage of barbiturates and the first dose of apomorphine is 1.2 mg. instead of the usual 0.6 mg. When the foregoing procedures have been effective in emptying the stomach, the patient receives the usual premedication and anesthesia. In the event that the preanesthetic preparatory procedures have been ineffective in emptying the stomach, the plan is to retain consciousness and protective reflexes by employing a regional analgesic block for the termination of labor and the completion of the delivery.

In cases requiring operative abdominal or other surgery during the course of pregnancy, the plan of premedication and anesthesia is decided upon an individual basis and after consultation between the surgical consultant and the anesthesiologist.

Hospitalized patients are not permitted food or fluid by mouth during labor. Fluids are administered parenterally, as indicated, to meet the patient's physiologic requirements.

Central-Nervous-System Complications

In premedication the drugs, dosages and routes are employed as for the uncomplicated case. Individualization is the basis in actual practice.

Regional analgesia and the use of solid anesthetic agents are contraindicated in this group of cases. An inhalational anesthetic procedure is planned for the following problem cases: patients with a previous history of headache or backache; patients with a suspected, or known, lesion of any part of the nervous system; and patients presenting a history of previous difficulty with regional anesthesia.

Metabolic Disturbances

Diabetes. The plan of premedication is essentially the same regarding selection of amnesic and analgesic drugs, but the dose is reduced so as to avoid loss of consciousness. The purpose is to utilize the aid of the patient during administration of a regional block for the termination of labor and delivery.

Hyperthyroidism. The agents employed for premedication are the same, but the dose is increased by one eighth to one fourth the amount, the interval and routes of administration remaining the same. The anesthetic procedure of choice is inhalation, employing oxygen-enriched atmospheres.

Specific Obstetric Complications

For patients who are to have cesarean section or "double set-up" examination to determine the cause of late antepartum hemorrhage, premedication consists of the administration of 0.2 gm. of sodium amytal by mouth, or rectum, two hours preoperatively; scopolamine and apomorphine, 0.6 mg. of each, are injected intramuscularly one hour later. The anesthetic procedure of choice is inhalation — otherwise, there is a consultation by the attending obstetrician and the anesthesiologist.

For patients presenting the problem of prematurity or suspected immaturity of the fetus, premedication consists of a minimal dose of a barbiturate, usually 0.1 gm. of seconal one hour before delivery, followed by a regional analgesic procedure.

For patients who are to have a test of labor, the plan of premedication is essentially the same as that for the uncomplicated case, but the dose of drugs is reduced by half. If the delivery is completed vaginally, the choice of anesthesia is an inhalational procedure. Otherwise the case is treated on an individual basis.

In patients with pre-eclampsia or eclampsia, if the case is one of mild or Grade I pre-eclampsia, premedication and anesthesia are planned as for the uncomplicated case to be delivered vaginally, in the absence of other complications. The severer cases presenting this obstetric complication are individualized. If premedication is employed demerol in doses of 50 to 100 mg. every three or four hours intramuscularly is administered and light inhalation anesthesia with highly enriched oxygen atmosphere is used for the delivery. When possible the delivery is completed under the premedication alone, any further depression or interference with vital functions being avoided. It is important to remember that a "whiff" of gas alone is a dangerous procedure. Intravenous anesthesia and nitrous oxide (or either procedure alone) are contraindicated for this group of cases. If regional anesthesia is to be employed, the decision rests on consultation between the attending obstetrician and the anesthesiologist. In any case the guiding principle is that safety must never be sacrificed for comfort or convenience.

Spinal Analgesia

When we employ one of the methods of regional anesthesia we are governed by the presence of a definite indication. This policy is best illustrated

by a brief consideration of spinal analgesia as currently used at the Boston Lying-in Hospital.

Indications

When the patient presents one or more of the following complications spinal analgesia constitutes the usual practice in the termination of delivery; respiratory complications, including fever or cough; a recent meal, when delivery is imminent and unconsciousness may be a threat to life; fetal distress, when further depression is best avoided; prematurity or immaturity of the fetus; diabetes mellitus, particularly if severe or uncontrolled; and other complications, such as a surgical procedure other than obstetric. The final decision rests between the attending obstetrician or consulting surgeon and the anesthesiologist.

Contraindications

We consider that the majority of obstetric cases fall in this group, and may be listed as follows: known or suspected disease of the central nervous system, such as tumors, hemorrhage or lesions of the brain or spinal cord, syphilis of the central nervous system, pernicious anemia involving the nervous system and other pathologic processes involving the parenchyma or coverings of the central nervous system; infection of the skin at or close to the point of spinal puncture; known history of headaches or backaches; mental aberrations such as psychoses and psychoneuroses or marked fears or anxieties; congenital anomalies — for example, pilonidal cysts and spina bifida — or other malformations of the structures about the spinal column; hemoglobin of 50 per cent or less; cardiovascular disease, labile vasomotor system or unstable autonomic nervous system; marked malnutrition, septicemia, hemorrhage or shock; known allergic responses to solid anesthetic agents, or previous history of undesirable experience with a regional anesthetic; marked obesity; serious uterine complications, such as uterine apoplexy, rupture and hemorrhage; necessary intrauterine manipulation — for example, internal podalic version or breech delivery; abnormal spinal fluid — turbid, cloudy or bloody spinal tap (also, patients with increased spinal-fluid pressure, for this may mean a block in the spinal canal); fear of post-spinal sequelae; and other patients so considered by the attending obstetrician in consultation with the anesthesiologist.

Technic and Agents

Evaluation of the patient, her disease, state of maturity of the fetus, and previous anesthetic experiences should be made. Premedication consists of the administration of 0.1 to 0.2 gm. of sodium amytal two hours prior to delivery and 50 to 100 mg. of demerol one hour later injected intramuscularly. The patient's blood pressure, pulse rate and respiratory rate and character are noted and recorded on the obstetric anesthesia study sheet. The patient is then placed in the lateral or sitting position and supported by an assistant. The skin over the lumbar portion of the back is prepared with ether, followed by tincture of zephiran, and sterile towels or sheets are applied. With sterile gloved hands the site of puncture is located, the third or fourth lumbar interspace being used. Ampoules are examined for cracks, only ampoules that are clear and colorless being used. A wheal is raised with a 0.5 per cent procaine containing not over 50 mg. of ephedrine sulfate. If an allergic response is elicited the spinal analgesic procedure is discontinued. Otherwise, the path to and including the interspinous ligaments is anesthetized. Flexible needles with short bevel and properly fitting stylets are employed for the spinal tap, the needle being tested before use. The bevel is inserted caudad. A spinal needle of 20 to 22 gauge is selected; if the needle is made of gold or platinum, the gauge should be 22 to 24. In the latter instance a groove director is previously inserted into the spinous ligaments. The needle is slowly introduced with the stylet into the dural sac and thence into the subarachnoid space. The stylet is carefully withdrawn, and clear fluid should appear. The procedure is discontinued if the spinal fluid is bloody, turbid or cloudy, or if under abnormal pressure. Otherwise, with the needle held fixed in place, the anesthetic solution is slowly injected at an approximate rate of 0.25 cc. per second. The anesthetist should always be on the alert for any untoward reactions. Our selection of agents is limited to the following:

For pelvic delivery procaine hydrochloride, 50 to 100 mg. in a concentration of not over 5 per cent is used, with spinal fluid as the diluent. The expected duration is approximately from one to one and a half hours and not infrequently longer. The height of sensory analgesia is governed by the rate of injection, dilution, amount of drug, interspace employed and positioning of the patient as the more controllable variables. We avoid barbotage. If saddle block is desired, injection is performed slowly, and the sitting position is maintained about 3 to 5 minutes, the level being frequently tested. For abdominal delivery the agent of choice is procaine hydrochloride, 100 to 150 mg. in 5 per cent dilution. The duration of effect may be expected for one to one and a half hours. If a longer duration is required, this being a teaching service, pontocaine hydrochloride (5 to 8 mg.) with procaine hydrochloride (50 to 100 mg.) is resorted to. In that case we prefer to limit the dose of pontocaine to 5 mg., and in any case the concentration of drugs injected is not over 5 per cent. At the end of the procedure the needle

is withdrawn, and the needle and syringe examined. A sterile dressing is applied to the puncture site. The patient is turned on her back, with one or two pillows under her upper back, neck and head. The level of analgesia is frequently tested, and the patient cautiously positioned, as indicated. The patient is leveled when the desired height is reached, that is, the tenth dorsal dermatome for pelvic deliveries and the sixth to the fourth dorsal dermatome for abdominal delivery.

Therapeutic and Prophylactic Measures

The clinical course of the patient is checked, and at intervals of at least five minutes the blood pressure, pulse rate, respiratory rate and volume are recorded. Intercostal breathing, the development of pallor and other skin changes, disorientation or other changes in behavior, nausea or emesis, thirst, air hunger, palpitation, precordial distress and other psychosomatic changes are watched for.

The patient is supplied early and immediately with air that is highly oxygen enriched. Carbon dioxide is avoided, for it only increases the vascular dilatation and augments spinal shock. An adequate airway is watched for and maintained; the thorax is inflated manually via the rebreathing bag with oxygen, should intercostal paralysis exist.

The use of the Trendelenburg position is avoided until the anesthetic agent is fixed — that is, for 25 to 30 minutes after induction.

Measures are instituted to support depressed respiration and circulation at once. Venoclysis or transfusion is employed promptly as indicated. During acute hemorrhage there is no substitute for compatible whole-blood transfusion.

Supplementary anesthetic agents and technics are employed when indicated. Adequate assistance, suction, oxygen, fluids, drugs (ephedrine sulfate, prepared) and indicated agents must be available constantly. The patient must be watched by the anesthetist responsible for the case, and knowledge must be had of all the patient's psychic, psychosomatic, somatic and reflex responses constantly.

Discussion

It should be emphasized that about 80 per cent of our deliveries are completed by the use of inhalational anesthesia. Under inhalational technics are included open-drop ether and semiclosed and closed carbon dioxide absorption methods, both circle-filter and Waters to-and-fro procedures. We stress the use of oxygen-enriched atmospheres, especially during the terminal portion of the second stage of labor. The delivery is actually accomplished in the topmost portion of the first plane of the third stage in accordance with Guedel's classification of the stages of anesthesia. The accumulation of carbon dioxide, even in the presence of oxygen-enriched atmospheres, is neither encouraged nor desired.

In another paper[2] several case histories of vaginal deliveries are presented as typical of our current practices of premedication and anesthesia. The drugs are essentially the same in all cases. The method of delivery with reference to the terminal anesthetic procedure is different in each case. The problems presented by each patient during her period of hospitalization are discussed in some detail.

Summary

The current practices of premedication and anesthesia at the Boston Lying-in Hospital are presented and discussed. Emphasis is placed upon the knowledge, experience, skill, judgment, attention and mutual professional confidence of the team, composed of the obstetrician and the anesthesiologist and their co-workers. The keynote is the practice of safe relief of pain, permitting application of a conservative policy in the conduct of labor. Over 80 per cent of our deliveries are completed under inhalation anesthesia. The advantages of inhalation anesthesia are discussed. An outline of the conduct of premedication and anesthesia with reference to the obstetric problem is presented.

The policy regarding regional analgesia is considered. An outline of indications, contraindications, technic, agents, therapeutic and prophylactic measures for spinal analgesia in obstetrics is included.

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FAMILIAL HEREDITARY HEMORRHAGIC TELANGIECTASIA IN THE NEGRO*

Report of a Case

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CHICAGO

BECAUSE familial hereditary hemorrhagic telangiectasia in the Negro has not been previously described in the literature, it was believed that the following case deserved mention.

A 48-year-old Negress first entered the Cook County Hospital on October 31, 1945, because of a nosebleed lasting 8 hours. She had had frequent epistaxes all her life, and 2 weeks before admission had noted vertigo, syncope and edema of the face and feet. The nosebleeds had occurred at intervals "as long as she could remember" but had been inconsequential until the menopause, at the age of 42. During the next 4 years they increased both in frequency and severity until at the time of admission she was averaging three episodes a week, each one lasting from 3 to 9 hours. There was also a history of bleeding from the tip of the small finger of the right hand on two different occasions about 1½ years previously. There was no recurrence of this bleeding after she learned to guard this spot from trauma. The menstrual periods were regular with a moderately heavy flow until the menopause. There had been no post-menopausal bleeding. She had been pregnant twice, one pregnancy terminating in a destructive operation because of a dystocia, and the other in the normal delivery of a healthy child.

The past history was eventful but had no relation to the present episode.

No familial history of bleeding could be elicited, with one exception, that of a brother, recently dead of "heart trouble," who had had moderately severe nosebleeds once or twice a year. Efforts to communicate with members of the family were unsuccessful. Inquiry into the racial background failed to reveal any known admixture of white blood, but the maternal grandmother was said to have been an American Indian.

Physical examination showed the patient to be well developed and well nourished; she appeared much younger than her chronologic age. She was intelligent and co-operative and did not appear acutely ill. There was continuous bleeding from the nose. The mucous membranes were extremely pale. Multiple small, bright-red areas varying in size, the largest approximately 3 mm. in diameter, were present on the tongue, buccal mucosa, gums, soft palate, face and chest. A similar spot was present under the tip of the nail of the small finger of the right hand. The lungs were normal. The heart was enlarged, the apical beat being visible 9 cm. to the left of the midclavicular line in the sixth interspace. A loud, harsh systolic murmur was heard over the entire precordium, but was loudest in the third interspace. The liver was palpable 7 cm. below the costal margin and was firm and smooth. A firm, slightly tender mass, about 3 or 4 cm. in diameter, was palpated in the right lower quadrant of the abdomen. On pelvic examination this was found to be connected with the right adnexa. Examination of the nose revealed bleeding from the right Kiesselbach's area. This was treated with silver nitrate, and the nose was packed.

The temperature was 98.6°F., the pulse 88, and the respirations 20; the blood pressure was 120/75.

Examination of the blood revealed a red-cell count of 1,560,000, with a hemoglobin of 13 per cent (2.0 gm.), and a white-cell count of 5050, with a normal differential. The red cells were microcytic and markedly hypochromic, with moderate anisocytosis and poikilocytosis. The bleeding time was 1 minute, 35 seconds, and the coagulation time 8 minutes (by the multiple tube method); prothrombin activity was 90 per cent; and the platelet count was 217,500. Urinalysis, blood Kahn and Wassermann tests and x-ray examination of the colon were negative. The nonprotein nitrogen, total serum protein and cevitamic acid determinations from time to time revealed no significant information.

Moderately severe epistaxes occurred at intervals during the following 10 days but were controlled by packing. The patient received 2000 cc. of whole blood during this period. She left the hospital on iron therapy on November 19 feeling well but still moderately anemic (on November 16 the red-cell count was 4,280,000, and the hemoglobin 72 per cent).

She was readmitted to the hospital on January 25, 1946, with a history of massive hemorrhages from the nose for several days. Physical examination was essentially the same as previously.

Examination of the blood disclosed a red-cell count of 1,080,000, with a hemoglobin of 11 per cent (1.7 gm.), and a white-cell count of 12,400.

The bleeding was again treated locally with silver nitrate, and she received 500 cc. of whole blood. As no further bleeding occurred during the next 10 days, she was transferred to the dermatology ward for treatment with moccasin venom intradermally. This she received twice weekly in doses ranging from an initial dose of 0.1 cc. up to 1.0 cc. In spite of this treatment the epistaxes recurred, became both frequent and severe, and required packing. Two 500-cc. blood transfusions were given during that time. On March 24 a new telangiectatic area was noted on the ball of the right thumb. On April 3 the patient was discharged to the dermatology outpatient clinic for further treatment.

The patient was readmitted to the hospital on September 3. There had been three severe nosebleeds since discharge, and she had experienced progressively increasing weakness, which had necessitated confinement to bed for the preceding 2 months. Nausea and vomiting had been present for 4 hours during the night before admission. Examination of the blood disclosed a red-cell count of 1,090,000, with a hemoglobin of 9 per cent (1.4 gm.), and a white-cell count of 7950. She was given 1000 cc. of whole blood immediately and placed on iron therapy. Further treatment was hampered, as in the past, by the difficulty of obtaining blood donors. Moccasin venom was continued in doses from 0.4 to 0.8 cc. Three weeks after admission she left the hospital against advice, although her condition was very little improved and she was still experiencing frequent and severe epistaxes.

She was again admitted on March 31, 1947, with complaints of edema of the face and legs for 2 weeks and epistaxis for 12 hours. The red-cell count was 1,600,000, and the hemoglobin 21 per cent (3.3 gm.). She was given a transfusion of 500 cc. of whole blood and rutin§ was administered in a dosage of 20 mg. four times daily. Only a few minor hemorrhages occurred during this hospital stay, and at the time of discharge from the hospital at the end of April the red-cell count was 3,210,000, and the hemoglobin 53 per cent.

On June 16 the patient re-entered the hospital after two severe nosebleeds during the previous 3 weeks. She had not been taking rutin during the interval because her supply was exhausted. The hemoglobin was again down to 23 per cent. Since no blood was available the patient was treated with iron and rutin only.

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§The rutin was furnished by the Abbott Laboratories through the courtesy of Dr. Richard K. Richards.

The patient was last seen on July 17, 1947, when the hemoglobin was 34 per cent and the red-cell count 3,120,000. She had experienced several slight episodes of bleeding since leaving the hospital. Rutin therapy is now faithfully followed.

Discussion

This patient presented the typical findings associated with familial hereditary hemorrhagic telangiectasia. The life-long history of nosebleeds, increasing in severity with advancing years, together with the presence of multiple telangiectatic areas on the skin and mucous membranes established the diagnosis without question. It is unfortunate that a definite familial incidence could not be traced. The history of the deceased brother who had nosebleeds is suggestive, but vague, and impossible to substantiate. The possibility that the patient had some admixture of white blood cannot be ruled out, of course, even though she had no knowledge of Caucasian consanguinity.

Whether the profound anemia was the result of the epistaxes alone, or the result of additional bleeding from lesions in the gastrointestinal tract is a matter for speculation, for such lesions do occur frequently. It was believed that the potential danger involved in gastroscopy of such a patient was too great to warrant the procedure.

Although no treatment is entirely satisfactory in these cases, the administration of rutin appears to have been of some benefit; the use of snake venom was apparently without avail.

Summary

A case of hereditary hemorrhagic telangiectasia occurring in a forty-eight-year-old Negress is presented, no previous report in a Negro being available.

The administration of rutin appears to have been of some value in this case.

MEDICAL PROGRESS

PLASTIC SURGERY

Skin Transplantation

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THE essence of plastic surgery is the transplantation of tissue. Skin is the one most commonly transplanted. It is therefore proposed to review the development of the methods of skin transplantation that have led to some of the modern principles on which the present management of plastic surgical problems is based. In any young surgical specialty much emphasis is placed on methods and technics, which, as they improve and are standardized, pave the way for the formulation of basic principles that apply in the broadest sense. Many of these principles bear directly on all phases of reconstructive surgery, but particularly on the surgery of trauma. Their elaboration has been stimulated by the concentrated experience of plastic surgeons in caring for war casualties, as well as by varied and extensive experiences in civilian reconstructive surgery.[1–4]

Skin transplantation is carried out in two basic ways: free transplantation or skin grafting, which means that the skin is completely detached from the body in its transfer; and transplantation as a flap, which means that at all times the skin and subcutaneous tissue remain attached to the body and receive blood supply through this attachment or pedicle. The free skin graft must be thin, without any subcutaneous tissue, to survive and grow after transfer, whereas the flap must retain the subcutaneous tissue in which the nutrient vessels of the skin lie.

In the primary or secondary closure of traumatic or surgical wounds and in the resurfacing of scarred areas, the simplest, most effective approach is desirable. Four principal methods are generally used, the indications for which are frequently emphasized in the papers reviewed for this report on skin transplantation. The first and simplest closure is by direct suture, which implies an adequate amount of healthy skin to allow approximation of the edges without tension. The second method is by a free skin graft. The split skin graft is readily available, and since the donor area heals within two weeks,[5] no additional deformity results. The graft will take on a well prepared granulating wound, such as that resulting from a burn, but may not survive on an avascular surface of scar tissue such as that underlying a thin layer of excised scar epithelium or that in an area with deep radiation damage. It will usually grow on cancellous bone but seldom on cortical bone.

The free skin graft has widespread usefulness as a primary skin dressing of large and small un-

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healed surfaces,[6, 7] in replacing damaged or lost skin,[8] in the closure of burn wounds after surgical excision,[9] in the resurfacing of superficial scars and release of deforming scar contractures[10] and in many other conditions. A free skin graft may have to be replaced with a flap, or a flap used primarily, when deeper structures such as bone, tendon or nerve are damaged, or when operation on these structures is contemplated. If the condition of the deep tissues will not support a graft — for example, in a deeply penetrating wound, or when the full thickness of a part, such as the nose or cheek, is missing — a flap must be used.

The third and fourth methods available for wound closure, resurfacing of a scar, or restoration of a part are the use of a local and a remote flap.[11] A local flap is desirable if sufficient skin is obtainable in the vicinity without interfering with function or creating additional deformity, and a remote flap is desirable if these conditions cannot be fulfilled or if larger amounts of skin are necessary. Flaps find their greatest usefulness in reparative surgery following compound traumatic wounds, either civilian or military. Usually there is damage and scarring of the deep structures, which delays their healing and disrupts their function. The restoration of surface covering[12, 13] and improvement in general nutrition of the part[14] are the first steps in the preparation for orthopedic or other surgical repair. The deep repair can be only as successful as the surface healing. In the absence of a part, not only skin but also subcutaneous tissue is necessary for bulk. Thus the destroyed nose, cheek, finger or ear is restored with one or more flaps.

Free Skin Grafting

The free transplantation of skin has been practiced only during the last seventy or eighty years. Reverdin, in 1869, first demonstrated that small bits of epidermis could be transplanted to unhealed surfaces in other parts of the body. According to Koch,[15] Lawson was the first to transfer a sheet of skin successfully, but Ollier, Thiersch, Wolfe and Krause are more often thought of in connection with the early development of methods in transplanting skin of intermediate and full thickness.

Little except a description of "small deep grafts" by Davis[16] was added to the technics and understanding of free skin grafting until after World War I. The challenge of the war and the increasing interest in the initial and late care of burns led to the development and perfection of methods for obtaining large sheets of skin and to a better appreciation of the conditions necessary for successful transplantation.

The modern concept of the use of free skin grafts had its beginning in 1929, when Blair and Brown[17] published the first of a long series of papers. These important publications were summarized in 1943 by Brown and McDowell[18] in a monograph. Their basic contribution was the description of a simple, efficient method for obtaining large sheets of skin. With the use of a long thin knife and a suction box to hold the skin taut, grafts as large as 90 by 10 cm. have been cut.[19] This method is still standard practice with many surgeons. A moderate amount of skill and experience is necessary for the effective use of this technic. Variations in the procedure, devised to minimize the human factor, have been suggested by Marcks[20] and Caltagironi. The introduction of the dermatome by the late Earl Padgett[21] in 1939 makes it possible for surgeons with minimal experience to have adequate amounts of skin available for grafting. The dermatome is an accurately machined half-drum with a knife blade attached by radial arms to the axis of the drum. The thickness of the skin graft, which is stuck to the drum by rubber cement, is determined by the distance between the edge of the knife blade and the drum. The method immediately received widespread acceptance. Donor areas not easily adaptable to the use of a knife are available as sources of skin with the dermatome. The value is obvious in extensively burned patients. Padgett[22] summarized his experience in a monograph published in 1942. Several improvements in the dermatome have been suggested, all following the same principle. Webster[23] uses pliofilm to back the skin graft on the drum, which simplifies separation from the drum and prevents shrinking and wrinkling of the graft. May[24] employs nylon cloth for the same purpose. Reese[25] has constructed a precision dermatome and uses a rubber sheet, called "dermatape" for backing of the graft. In my experience, this is the most accurate and effective machine for cutting skin grafts yet introduced. Douglas,[26] by attaching a windshield wiper to the dermatome, mechanically supplied reciprocating motion to the knife.

As mentioned above, the most important and most frequent use of the skin graft is in the covering of unhealed wounds. Although many of these are the result of burns, it is not the purpose of this paper to discuss the early care of burns. Success in the skin grafting of raw surfaces depends to a large extent on management before and after operation. Seldom is a raw surface sterilized before grafting. The aim of the surgeon is to have firm flat granulations without cellulitis and with minimal drainage and minimal bacterial growth on culture. To achieve this goal, particularly in extensive areas, requires more than merely local therapy. The importance of maintaining normal protein, vitamin and electrolyte levels in the blood and a normal red-cell count and hemoglobin has been repeatedly stressed.[27–30] This necessitates frequent transfusions and other supportive measures to replace cells, protein and vitamins deficient in the all too often seriously debilitated patient.[31–33]

Cleanly care of the wound itself is also important.[34] Frequent change of dressing, scrupulous removal of crusts, exudate and debris, and application of moderate pressure will change the appearance of a wound completely. Saline tub baths have been used frequently by Brown,[18] and by Allen and Koch[32] to aid in the preparation of large raw surfaces for closure with skin grafts. Brown[18] has emphasized the importance of the use of fine mesh gauze against a granulating surface. This prevents the growth of granulations into the meshes of the gauze and thus reduces the likelihood of bleeding at the time dressings are changed. He has also introduced the use of the short fiber mechanic's waste, a universally available material and one that is just as effective as the more expensive sea sponges or fluffed gauze. Mechanic's waste can be made to mold itself against an uneven surface better than other materials and furnishes the resiliency needed for immobilization and support of the granulations and the later skin graft. Antibiotics and chemotherapy are, of course, very valuable aids but cannot supplant meticulous care of the wound.

The following is a brief summary of the management of skin grafts based on the reports of those who have had the widest experience in their use. The grafting of a raw surface is undertaken only when the patient's general condition is stabilized and when the granulating surface is firm and free from active infection. This condition can be judged best by clinical evaluation of the wound.[35] If the granulation tissue is thin and firm, it may be unnecessary to disturb it, but usually in long-standing ulcerations or old burns it is thick and irregular and should be carefully and smoothly shaved off.

The split thickness graft obtained either with a knife or by a mechanical device is the most satisfactory graft for healing granulating wounds or for large repairs. If adequate fixation of the graft is possible with the dressing alone, the grafts can be "snubbed" in place. Otherwise, suturing may be desirable. Sometimes the Reverdin or "pinch graft" may be used but this leaves a mottling of both the donor and the recipient site. Sheets of skin cut up into small pieces of postage-stamp size and held against the raw surface by the dressing are also useful.

Either grease gauze or wet fine mesh gauze is used immediately over the graft. Support of the graft and immobilization of the part is obtained by a bulky dressing of mechanic's waste and, if indicated, a splint.

A change of dressing is usually done by the fifth day if the grafted surface was granulating. This permits inspection of the operated area, removal of any marginal necrotic skin and mechanical cleaning of the surface. If the operated area was healed, the first dressing need not be done so early; the exact time is a matter of individual preference. All subsequent dressings are planned according to the condition of the grafts.

In the late care of skin grafts, supportive bandages are necessary. This is particularly true of the lower extremity until normal vasomotor tone is reestablished. In large grafts this may take six to eight months. For the upper arm, where the column of blood is not long, only a short period of support is necessary. In grafts for contractures of the neck, MacCollum[36] has recommended the wearing of a Thomas collar to stretch the graft.

Marginal scars, in elective skin grafting following the release of contractures or following surgical excision, must be so placed that a contracture will not develop or recur. This may be done by incisions or "darts" extending out from the margin, which are grafted with the central defect. Or, should there be such a contracture, it can often be released by a local shifting of flaps or Z-plastic.

Skin grafts have proved useful in extremity wounds with chronic osteomyelitis and large bone cavities. Among others, two valuable reports concerning this complex problem have appeared. Knight and Wood[37] have followed a three-stage procedure in obliteration of bone cavities: a thorough sequestrectomy and excision of all adjacent scar tissue; early split skin grafting of the cavity; and excision of the graft, filling the cavity with bone chips, and immediate closure with a flap either direct or prepared earlier. Kelly et al.[38] using the same procedure in the first two stages, have found that a third stage is often not required. Their results with bone grafting of the cavity have been disappointing and they prefer using a thick abdominal flap with abundant fat to fill it. They emphasize the importance of the vascularity of the final skin covering and the limited usefulness of chemotherapy and biotherapy.

Brown and McDowell[39] have reported follow-up studies on a large group of skin grafts in children. They find that the grafts grow, and function persists throughout the child's development.

A recent study of sensory regeneration in transplanted skin by McCarroll[40] confirms the clinical impression that the rate of return is inversely proportional to the thickness of the transplanted skin. Pain sensation returns sooner than touch, and the temporal dissociation is greater with a thicker graft.

Conway[41] reports a qualitative study of sweating function in transplanted skin. There is sweating only when the full thickness of the skin is transplanted. In thinner grafts, the functioning portions of the glands are apparently destroyed.

Space does not permit a more detailed presentation of the many recent publications about skin grafting. Methods and principles in using skin grafts, perfected largely by American plastic surgeons, have been so simplified that they are now generally available. The successful use of these

technics in skin grafting should make possible the prompt healing of burns, the immediate closure of most traumatic or surgical wounds and the early repair of deforming scars and chronic ulcerations.

In 1943 Sano[42] described a method of adhesive fixation of skin grafts to a raw surface. By mixture of a specially prepared plasma solution with leukocyte extract a fibrinous adhesive coagulum is formed that eliminates the need for a dressing or suturing the graft. The leukocyte extract is "painted" on the graft, and the plasma solution on the recipient surface before the graft is applied.

Several other methods of fixation of skin grafts and for "gluing" severed nerves were suggested, and there are still occasional reports of the value of these methods.[43, 44]

Young[45] reports fibrin fixation of skin grafts by the addition of thrombin to the recipient area and plasma to the graft. A clot forms when the two are brought in contact. He concludes that the method has value in applying grafts to fresh surgical wounds, for holding grafts while compression dressings are being applied, and as a means of holding small grafts that are not to be held with a dressing. He does not recommend the use of fibrin fixation for granulating wounds.

Brown[46] cites his use of coagulum fixation of skin grafts to a granulating surfaces. In each case a graft without adhesive substance was applied as a control. None of these grafts were sutured in place, and there was a complete take of all the grafts, including the controls. Brown reports the observation of many surgeons performing skin grafts to granulating surfaces that spontaneous adhesion occurs if the graft is pressed against the raw surface for a few minutes.

An interesting suggestion explaining the value of adhesive methods in skin grafting has come from Medawar.[47] He points out that the lower the temperature the less enzymic autolysis occurs and the less the risk of loss of the dormant graft from infection. Fixation with bulky pressure dressings tends to keep the graft at a higher temperature and increases this danger. The adhesive method, without a dressing, allows the graft to remain at a lower temperature and favors its survival. This technic of open grafting was used successfully for many years by Porter and Greenough at the Massachusetts General Hospital, without, however, adhesive fixation of the grafts.

Full Thickness Grafts

Wolfe–Krause or full thickness grafts, consisting, as the name implies, of the epidermis and full thickness of the dermis, have several advantages over grafts of intermediate thickness. One of the clearest and most complete expositions of the value of and indications for the full thickness skin graft has been presented by Byars.[48] Two important advantages of these grafts are emphasized: the minimal tendency to contract and wrinkle, and better color and texture of the surface. Full thickness grafts are harder to prepare and tedious to apply. They are more liable to failure, and the amount that can be transplanted is limited. The donor site must often be closed with a split skin graft. The advantages of these grafts are the reasons for their use.

Flexion is the functional motion of the hand so that little active stretching of the palmar skin occurs. Skin resurfacing of the palm is thus often best done with a full thickness graft that shrinks little. The same principle may apply in the definitive release of contracting scars of the neck. On the face there are delicate motions of expression, and the skin is exposed, so that both functionally and cosmetically the full thickness graft is preferred.

Full thickness grafts are usually taken from the groin, inner surface of the upper arm or abdominal wall. Skin from the fold behind the ear is available in small amounts and usually matches the skin of the face. Skin from the upper eyelid has been used by Wheeler[49] for repairs of the lids. A recent suggestion by Brown and Cannon[50] of full thickness grafts from the base of the neck has proved valuable because the grafted skin matches that of the face well, it is available in large amounts, and its function in kinetic areas of the face cannot be distinguished from the normal. An explanation for this observation is that only in the neck is there skin whose normal environment overlying the platysma muscle is similar functionally to the skin of the face, beneath which lie the delicate muscles of expression. In resurfacing the dorsum of the fingers to prepare for definitive tendon surgery, this graft has been used because of the loose areolar tissue beneath it in which the tendon will glide.

If a graft on the face fails to match the color of the adjacent skin, the color can be changed by permanent pigment injection, the same method used in tattooing. This technic of skin pigmentation was first described by Hance[51] and Byars.[52] It is not only of value in tinting grafts but also in masking the redness of capillary hemangioma or port-wine stain.[53, 54] The mixed pigments in the form of a thin paste are imbedded in the dermis by multiple puncture using fine cambric needles. The puncture is done either by hand or by a vibrating device.

Brown and Cannon[55] have described the composite graft from the ear for alar and columellar repairs. The graft, which comprises two layers of skin with the cartilage between, makes possible tissue replacement about the nostrils in a single operation. Minimal deformity of the ear, which can be repaired with local tissue, results. Dupertuis[56] has independently used segments of the ear lobe for similar repairs, particularly on the tip of

the nose. The composite graft has been used by Armstrong and Garcia[57] in repairs of the eyelid margin.

Homotransplantation

Ever since the first free skin graft was used the possibility of transplantation from one person to another has been the cause of much speculation and investigation. At the turn of the century there were isolated reports of successful isotransplantation or homotransplantation of skin. Davis,[58] in his monograph on plastic surgery in 1919, reported a review of hospital records and concluded that such homotransplantation was possible. Later, he was convinced that the observations were faulty. One of the most enlightening reports on this whole problem is that of Loeb,[59] a pioneer in tissue culture. Loeb considered individual biologic differences to be very specific. The more closely related the species, the less marked the individuality differential, which he characterized as chemical differences in the cells. In isografting these differentials come into play, and the evidence indicates that a primary substance or toxin is produced by the graft that causes a reaction in the host, making the graft disappear. That this is not a true immune reaction is indicated by Loeb's observation of the absence of an accelerated reaction on secondary transplantation. Studies by Medawar[60] shed further but somewhat different light on the subject. He presents contradictory evidence that the reaction to a homograft is a true immune phenomenon, with acceleration in proportion to dosage of the reaction to a second graft. Medawar also reports no evidence that red cells and skin share similar antigens, although leukocytes and skin do share them. Such an observation disproves the value of blood typing in homotransplantation. Barker[61] doubts that failure of homotransplantation is on the basis of sensitization to homologous skin proteins.

Stone,[62] in 1934, stimulated interest in homotransplantation by his studies of tissue culture of the parathyroid glands. He investigated the possibility of adapting the graft by first growing it as a tissue culture in a medium containing the body fluids of the future host. "This we have done in all cases in which we have secured successful grafts," he writes.

Both Padgett[63] and Brown[64] have reported successful homotransplantation of human skin in identical twins. An elective interchange of full thickness grafts on the upper arm was carried out by Brown. One of the most recent reports was that by Converse[65] in which one of twins was severely burned in the leg, and skin from the twin brother was used with the patient's own skin for covering. The behavior of the homografts, he reports, did not differ from that of the autografts, and a two year follow-up confirms the stability of the homografts. These observations of successful transplantation between identical twins suggests a very fundamental individual cell specificity. However, the fact that practically inert lymph-nourished tissues like cartilage and cornea can be permanently transplanted indicates that it pertains only to the more highly involved tissues of the human body.

Recent studies by Longmire[66] confirm the temporary survival of homotransplants and the insignificance of blood group of donor and recipient in skin homografting. He also presents evidence that, unlike blood types, skin types do not exist.

Barker[67] reports studies of pigment changes in iso skin transplants between black and white rabbits. Black skin is transplanted to white animals, and white skin to black. White skin on the black animal is completely pigmented in sixty to one hundred and twenty-nine days. Hair color remains unchanged up to five months despite a change in the color of the skin. Pigmentation of the white skin surrounding a black graft likewise occurs.

The chief clinical interest in homotransplantation is as a life-saving measure in badly debilitated patients with extensive burns. The homografts are used as a temporary skin dressing until the patient's condition warrants the use of autografts.[19] This method of homotransplantation has been successfully used for large granulating wounds in a badly debilitated burned patient. Skin was removed from a cadaver six hours after death and applied to the recipient seven hours later. The cadaver had been refrigerated and was cold when the grafts were taken. The grafts were wrapped in a moist sponge and left refrigerated until used.[68] The three-month survival period of these grafts is one of the longest on record. Unfortunate false publicity has led to the useless taking of skin from donors, who are led to believe that their skin will survive permanently. Skin banks have even been proposed. The occasions when homotransplants are indicated are very rare.

Transplantation of Flaps

The transplantation of flaps is one of the oldest of all surgical technics. Plastic surgery can thus claim its origin centuries before the Christian Era. War injuries, accidents and punishments and the ever-present congenital deformities have always provided a stimulus for the development of reparative surgery. Both Davis[69] and Koch[15] have reviewed the early history of skin transplantation and paid tribute to those who paved the way to modern plastic surgery. According to Davis, the Hindus (750 to 800 B. C.) were the earliest recorded practitioners of real plastic surgery. They understood the local shifting of skin flaps or sliding flaps that later somehow became known as the French method. Other technics, such as the repair of a nose with a forehead flap, were developed by members of the lower castes in India who in-

herited surgical practice when it came to be thought unclean. Today the use of a flap of forehead skin for nasal reconstruction is spoken of as the Indian method. This method was brought to the United States by Warren[70] after a sojourn in Europe and described by him in 1837. Another important method of nasal reconstruction, using a flap from the upper arm, has come to use from the writings of Taliacotius[71] of Bologna, whose face is engraved on the certificate of the American Board of Plastic Surgery. In 1840 Warren[72] again wrote about nasal reconstruction. He pointed out the value of this flap in avoiding a deforming scar of the forehead. Today, this type of nasal reconstruction is known as the Italian method.

The tubing of a flap as a preliminary to its transfer was reported independently by Gillies[73] and Filatoff,[74] but Gillies was its greatest proponent. Through his writings and his disciples, who carried his teachings to many parts of the world, the method gained widespread recognition and popularity. For the first time multiple-stage migration of flaps to remote parts of the body was possible. The skin surface remained closed at all times, and the hazard of infection and thrombosis was reduced.

Webster,[75] in 1937, described the thoracoepigastric tubed pedicle flap, which utilized for blood supply the long thoracic, the superficial thoracic and the superficial epigastric arteries and thoracoepigastric veins. These vessels lie subcutaneously on the abdominal and chest walls and are thus included within the substance of the flap. Large flaps of this type have proved useful for many types of surgical repair on many parts of the body.

That the use of tubed pedicle flaps is not without hazards, however, is indicated by Macomber and Rubin,[76] who list the precautions in the preparation of tubed flaps and the complications that may arise in their preparation, delay and transfer. These include necrosis from tension or from excessive length, hemorrhage within the tube, infection, improper timing of delays, kinking or angulation of the tube, use of an inadequate flap and improper closure following delays and several others. This report is based on a series of over 300 cases of tubed flaps prepared for repairing complicated war wounds of the extremities.

To reduce the possible complications in the preparation of tubed flaps, Shaw and Payne[77] have found it advantageous in applying small flaps to the hand to tube the pedicle at the same time. This method combines the speed of the abdominal flap with the cleanliness of the tube. Macomber and his associates[78, 79] have re-emphasized the value of a skin graft in the bed from which a tubed flap is prepared as a means of primary wound closure. The free skin graft is also useful in closing the donor area and undersurface of large direct abdominal flaps.

The forehead flap, or Indian method, has found increasing usefulness today in the repair of surgical and traumatic cases not only of the nose[80] but also of other parts of the face (eyelid, lip, mouth, orbit, cheek and chin). Blair et al.[81] report from a wide experience with this type of flap in repairs of the face following radical surgery for cancer. The authors describe the methods used, and the principles underlying their use are illustrated in detail. Various descriptions of flaps for facial repairs have been presented by other authors.[82–85] The major disadvantage of the forehead flap is the deformity that results. Since a normal feature is destroyed, this flap should be avoided in young people. In a large Army plastic center, the arm flap, or Italian method, was used almost exclusively in nose reconstruction for this reason.[86]

New[87] has described the "sickle flap" as a method that minimized the deformity. The skin for the repair is taken high in the temple along the hairline. The flap is carried on a sickle-shaped pedicle extending upward along the temporal artery and lying completely within the hairline. Very large repairs are possible by this method, including the nose, lip, eyelid or cheek.

Kazanjian[88] has described the "median forehead flap," which is elevated from the midline of the forehead and carried on a pedicle between the brows. The vertical scar in the forehead is not deforming. A surprising amount of skin can be mobilized by this method, which can be used in repairs of the eyelid, nose or upper lip.

The "island flap," devised by Gursnay in 1887 and later presented by Monks[89] in 1898, also leaves no deforming scars. Only two vessels, branches of the temporal artery and vein, form the pedicle of the flap, which can be either hairless forehead skin or hair-bearing scalp. The vessels are identified by palpation and dissected free through an overlying linear incision. The mobilized flap and vessels are passed through a tunnel to the recipient area. This flap is most useful for the eyelids and brow.

Large flaps from the anterior portion of the neck and chest wall are also used in facial repairs to avoid any additional deforming scars of the face. These methods have been described and utilized by many authors.[90–92] Flaps from the neck have the additional advantage of matching facial skin in color and texture. Brown and Cannon[93] describe a large flap with the base above the clavicle that lies vertically down the chest or crosses to the opposite side above the nipple level. This flap provides a method of obtaining large amounts of skin for the face without the need of migration in multiple stages.

A very useful direct method for repairs about the mouth is the vermilion-bordered lip flap, originally described by Estlander[94] in 1872. This flap, comprising the full thickness of the lip, is carried on a

narrow pedicle containing only the coronary artery and vein that encircle the lip. Rotation of the flap through 180° is possible. Its greatest usefulness is in direct closure after excision of the lip for cancer and in secondary repairs for harelip or trauma.[95–97]

Brown and his associates[12, 13] have emphasized the value of more direct methods in the transfer of flaps in preference to the slower delaying and tubing technics. By providing an adequately broad base with a short pedicle the viability of the flap is assured. The flap can be accurately prepared to fit the defect resultant from trauma or surgical excision of scars and attached at the same time. This direct transfer may save many weeks or even months of hospitalization and disability. This method has proved of value not only for the upper extremity but also, surprisingly enough, for the lower extremity. Either the thigh or the calf can be the source of these flaps for the opposite leg if local flaps are inadequate.

For more extensive resurfacing of the lower extremity or other parts, open jump flaps from the abdominal wall carried on the forearm have been described.[98, 99] Edwards[100] has compared the experience in 26 cases of open jump flap with a similar series using tubed flaps also carried on the forearm. The 26 jump flaps took an average of one hundred and six days and six operations to complete, and none were lost. Thirty-five tubed flaps were started, and 9 failed, so that only 26 were completed. An average of three hundred and thirty-three days and ten operations were necessary for the repair.

The application of the principles of plastic surgery to problems of general surgery is well demonstrated in the recent articles on decubitus ulcers in paraplegia and in repairs of the chest wall following very radical surgery.

Barker[101] reports that excision and suture or the advancing of flaps has proved satisfactory in the closure of decubitus ulcers. Grafts are reserved for patients whose condition does not warrant the use of flaps. Gibbon and Freeman[102] report experience with 65 patients with decubitus ulcers treated by excision and closure by advancing local skin flaps. White and Hamm[103] describe 14 cases of decubitus ulcers in patients with spinal paraplegia in which repair was accomplished by the rotation of local flaps. A trend toward the use of rotated flaps rather than advancing of flaps through stellate incisions is noted in the more recent writings. This is emphasized by Conway,[104] who says "large ulcers are closed successfully in the highest percentage of cases when a flap of skin and subcutaneous tissue is rotated from an adjacent area and the defect at the site of procurement of the flap surfaced by a free graft of skin." The important additional factor in success of removing all bony prominence is stressed by Kostrubala.[105] I have found this to be true in my experience with decubitus ulcers and in several cases have excised the outer table of the sacrum, removing with the bone all avascular and necrotic ligamentous and fascial tissue and leaving a base of healthy cancellous bone.

Both Maier[106] and Pickrell[107, 108] have reported the use of rotated flaps from the thoracic or abdominal wall and the skin of the breast and, in Pickrell's report, the use of free skin graft on the pericardium, for repairs of large defects of the chest wall following radical resection of tumors, resection of areas of radiation necrosis and in repairs following trauma.

Summary

An attempt is made to review early and recent developments that have led to present understanding of skin transplantation. Some of the principles of repair that have evolved with the perfection of methods and technics are presented. In the future, the development of direct methods and a more widespread understanding of basic principles throughout the surgical profession can be expected. Studies in wound healing and homotransplantation may cast further light on these puzzling problems.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

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CASE 34381

PRESENTATION OF CASE

A seven-year-old girl was admitted to the hospital because of pain and swelling of the left ankle.

The mother dated the illness back four months at which time the girl struck her left ankle and subsequently developed a slight limp. Four months before admission swelling was noted for the first time, and the ankle became painful. The pain gradually became more severe. Three months before admission the patient was said to have been feverish, although the temperature was not taken. X-ray films were taken by a physician, who made a diagnosis of Brodie's abscess.

On examination there was marked dental caries. There were bilateral palpable shotty inguinal nodes which were not tender. There was a 5-cm. by 7-cm., firm, slightly tender swelling of the anterior medial aspect of the left ankle that seemed contiguous with the lower end of the tibia and did not appear to cross the ankle joint. The foot was held in valgus position, although flexion and extension were normal as compared to the opposite side. The left medial malleolus was lower than the right. Measurements from the midpatella to the medial malleolus were, on the right, 9⅜ and, on the left, 9⅞ inches. The circumference of the leg, measured 1 inch above the medial malleolus, was right, 6½ and left, 7 inches. There was no remarkable redness or increased heat. There was no bruit. The temperature was normal.

Laboratory examination revealed a normal urine, a hemoglobin of 11.8 gm., a white-cell count of 8200 and a normal differential. The blood calcium was 8.8 mg. per 100 cc., the phosphorus 5.3 mg. per 100 cc., and the alkaline phosphatase 5.5 units per 100 cc. The total protein was 6.7 gm. per 100 cc. The sedimentation rate was 16 mm. in 1 hour. The blood Hinton and tuberculin tests were negative.

An x-ray film showed a rarefied area within the cancellous portion of the distal end of the tibial diaphysis, more toward the medial side (Fig. 1). The rarefaction extended to the metaphysis and also seemed to involve the cortex of the bone in one area. There was some suggestion of local decalcification within the adjoining epiphysis. Soft-tissue swelling was present, and there was some periosteal new-bone formation along the medial aspect of the distal tibia. There were no lesions in the spine, pelvis, skull or lungs. Measurement of teleroentgenograms showed ¼-inch lengthening of the left tibia.

FIGURE 1.

On the seventh hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CHANNING C. SIMMONS: According to the x-ray films this patient has an area of bone destruction with slight periosteal proliferation in the lower end of the left tibia. It can be noticed that this tibia is slightly larger than the other. It is a question whether the lesion extends across the epiphysis or whether the appearance in the film is due to rarefaction of disuse. The lymph node in the groin, I think, is of very little significance.

Diagnosis of these bone tumors, as I have said many times, lies between a diffuse skeletal disease, an inflammatory condition, and some form of tumor. From the data at hand, I think we can fairly well rule out a general skeletal disease. Inflammatory conditions such as syphilis, tuberculosis and osteomyelitis are all possibilities. The blood Hinton

test was negative, which pretty well rules out syphilis, although bone syphilis might give a negative Hinton test. An inflammatory condition has to be considered — a Brodie's abscess, so-called, or localized osteomyelitis. We have to consider osteogenic sarcoma, Ewing's sarcoma, plasma-cell myeloma, eosinophilic granuloma and giant-cell tumor.

An inflammatory condition in a child usually is found in the epiphyseal region, which is stimulated, causing the bone to grow longer as in this case. Whether tumor in the same situation will do this, I do not know. However, the normal temperature militates against an inflammatory condition. Of the tumors, osteogenic sarcoma may be present. It is rarely found in this position or gives this picture, although osteogenic sarcoma can simulate any condition. Giant-cell tumor gives a picture of bone destruction without new-bone formation, but there was new-bone formation associated with this lesion. Eosinophilic granuloma I should not consider. Plasma-cell myeloma is usually a multiple disease, although single bones are occasionally involved. Ewing's sarcoma may perfectly well give this picture of destruction but usually with much more tumor clinically than is suggested by the x-ray film. In other words, the whole leg is enlarged. Ewing's sarcoma may give a little fever or a slightly elevated white-cell count.

I think, frankly, that it is impossible to make a diagnosis. It would lie between an early giant-cell tumor and an inflammatory condition, such as Brodie's abscess. The only way to make a diagnosis definitely in this case would be to do a biopsy and let the treatment be governed by what was found. Whether or not it would be possible to do a suction aspiration biopsy, I do not know.

DR. STANLEY M. WYMAN: From the radiologist's point of view, everything Dr. Simmons has said is entirely correct. My own feeling about it is that the chief thing to decide is whether the lesion is inflammatory or neoplastic; and if neoplastic, whether it is benign or malignant. In favor of infection are the soft-tissue swelling, the elongation of the bone, the periosteal reaction and the circumscription of the lesion without any perceptible or gross reaction about the lesion. I think I should place inflammation of low grade as my first bet.

DR. BENJAMIN CASTLEMAN: Are there any other suggestions?

A PHYSICIAN: How often does a giant-cell tumor occur in this age group?

DR. CASTLEMAN: According to Jaffe* one does not see it before twenty.

DR. LAURENCE L. ROBBINS: Oh, yes you do; I have seen it in patients around fourteen.

DR. CASTLEMAN: I do not believe I have seen one in a child of seven.

*Jaffe, H. L., Lichtenstein, L., and Portis, R. B. Giant cell tumor of bone: its pathologic appearance, grading, supposed variants and treatment. *Arch. Path.* 30:993-1031, 1940.

DR. ROBBINS: We do not see them until the epiphysis is closed because they are usually in the epiphysis.

CLINICAL DIAGNOSIS

Bone sarcoma?
Brodie's abscess?

DR. SIMMONS'S DIAGNOSIS

Benign giant-cell tumor?
Brodie's abscess?

ANATOMICAL DIAGNOSIS

Brodie's abscess of tibia.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At operation the surgeon exposed a trap door in the cortex and curetted some material that appeared grossly to be chronic inflammatory tissue. On microscopical examination we found an exudate of polymorphonuclears, lymphocytes, monocytes and plasma cells that would fit in with a Brodie's abscess. Culture showed *Staphylococcus albus*. The patient is doing well.

DR. SIMMONS: What was the preoperative diagnosis in the ward?

DR. CASTLEMAN: It varied. Everyone who examined her had a different diagnosis. On the anesthesia sheet the preoperative diagnosis was given as sarcoma of the lower tibia, but several members of the orthopedic staff said it was a Brodie's abscess. Neurofibroma was also suggested because the leg was longer on one side.

CASE 34382

PRESENTATION OF CASE

First admission. A forty-year-old woman was admitted to the hospital because of persistent phlebitis and ulcers on the lower legs. The phlebitis had commenced twenty-five years previously following an appendectomy, had recurred following childbirth eleven years later, and a bilateral high saphenous ligation was done after another five years. Seven years before entry, again following childbirth, there was an attack of phlebitis of the right arm. The legs were not involved. Since then there were recurring ulcers on the lower legs. One year before entry because of swelling around the hips, thrombosis of the pelvic vein was diagnosed.

The patient was well developed and well nourished. Examination of the heart, lungs and abdomen was negative. There was no edema of the legs although they appeared swollen and the skin was tense. There was no palpable arterial pulsation below the femoral veins. There were ulcers on the medial aspect of both legs, around and above the malleoli.

The temperature and pulse were normal.

Laboratory examination revealed a normal urinalysis. The clotting time varied between 20 seconds and 2 minutes and 5 seconds. A bilateral lumbar sympathectomy was done, and communicating leg veins were ligated.

Second admission (three months later). Following the operation the patient did well until she developed an acute maxillary sinusitis. She noticed some painless swelling of both lower extremities at this time. Three days after the onset of the sinusitis she noted left-sided back pain on breathing. She developed a cough, fever and bloody sputum. On readmission to the hospital the chest findings, including x-ray examinations, were consistent with pulmonary infarction. The clotting time was 5 minutes, and the prothrombin time 27 seconds (normal, 22 seconds). Venograms showed no filling of the deep veins in either leg. A ligation of the inferior vena cava in continuity was done.

Third admission (two years and five months later). Following the vena-cava ligation the patient had bilateral varicose ulcers, which kept breaking down. A bilateral femoral-vein ligation was done at this time, and a dilatation and curettage were performed; x-ray treatment (1000 r) was given to stop menstrual bleeding.

Fourth admission (fourteen months later). In the interval the patient's condition was unchanged, and the leg ulcers continued to break down if the patient walked excessively. Three months before admission the patient developed shingles around the buttocks. This subsided but six weeks before admission an abscess the size of a billiard ball developed over the lower spine. This broke spontaneously and subsided.

On examination there were moderate external hemorrhoids, but there was no pilonidal dimple. A hemorrhoidectomy was done.

Fifth admission (one and a half years later). Ten days before admission the patient noticed a steady gnawing pain under the tip of the xiphoid. This persisted and became more severe and shifted to below the original site. The pain was aggravated by movement and only partially alleviated by rest and medication. The pain radiated to the upper lumbar region and back. There was no nausea, vomiting or anorexia. The bowel movements were regular, and there was no melena. There were no chills, no fever and no bouts of crampy pain. There was no weakness or weight loss.

On examination there was some vague, not localized, slight abdominal tenderness.

The blood pressure was 116 systolic, 70 diastolic.

Examination of the blood disclosed a white-cell count of 14,200, with 81 per cent neutrophils. The platelets were somewhat decreased. The serum amylase was 13 units, and the prothrombin time was 18 seconds (normal, 16 seconds). The specific gravity of the urine was 1.012. There was a + test for albumin and the sediment contained an occasional red cell and 25 white cells per high-power field. The stool was guaiac negative.

The pain was much relieved by the third hospital day, and the patient was taking fluids comfortably. A gastrointestinal series, Graham test and barium enema were negative.

During the evening of the fourth day there was an exacerbation of pain with vomiting of recently ingested water. Abdominal tenderness was not well localized to either side of the abdomen. There was no spasm or distention. The vomiting continued, and the maximum pain and tenderness shifted to the right, chiefly in the upper quadrant. There was a sense of resistance to palpation on the right. The temperature was normal. The abdomen was quiet on auscultation, and an occasional normal peristaltic sound was heard. There was no change in the sound with exacerbations of pain. On the fifth hospital day severe pain, nausea and vomiting recurred and persisted, and the tenderness was constantly referred to the right lower quadrant.

An operation was performed.

Differential Diagnosis

Dr. Arthur W. Allen: Have you some films of the abdomen? May we see them now?

Dr. James J. McCort: Do you want to see the early films of the infarct?

Dr. Allen: I do not know that we need to. I am more interested in the films of the present illness. You probably have a plain film of the abdomen taken shortly after admission.

Dr. McCort: No; we do not have that. These films you see are of the gall bladder on the last admission, and the gall bladder is seen to concentrate the dye well. No calculi are present. This is the barium enema. There is no definite abnormality demonstrated in the large bowel. There is only slight filling of the terminal ileum on this examination. There are no defects, and no evidence of

dilated loops of small bowel, although some loops contain air.

DR. ALLEN: There is a small shadow to the right of the spinal column. Does that have any significance at all?

DR. MCCORT: I do not know the significance of the small calcification in the right lower quadrant.

DR. ALLEN: Is it anywhere near the course of the ureter?

DR. MCCORT: It seems a little bit lateral. I cannot rule out a ureteral calculus without a urogram, but it may be a calcification in a mesenteric lymph node.

The films of the gastrointestinal tract were taken at the time the barium was ingested, and no abnormality is demonstrated in the stomach or duodenum. This film was taken six hours after the barium was administered, and the stomach is completely empty. The greater portion of the barium is present in the lower small bowel and ascending colon. A narrowed area, several centimeters in length, is present in the terminal ileum. This might bear further investigation to determine whether it is a tumor or inflammatory stricture.

DR. ALLEN: Is that in the ileum?

DR. MCCORT: Yes.

DR. ALLEN: This patient is interesting from many points of view, and since I have no clear-cut idea as to what brought her in here the last time, I think I am justified in reviewing some of the points of the past history. In the first place it appears that this woman developed her original thrombophlebitis at the age of fifteen. This is unusual because although we do see this complication following injuries to the lower extremities in young people, such as burns and fractures, it is rare to have it occur as a complication of an appendectomy or any such operation as that. Without a doubt she had a rather fulminating attack of bilateral femoral phlebitis at that time. It is common to have in these patients a recurrence of their thrombophlebitis following childbirth or operation, and she proceeded to behave in this characteristic fashion. The story brings out a good many of the methods of examination and treatment of chronic thrombophlebitis that we used in previous years but now are not using at all. For instance, before this woman had an interruption of the femoral vein, she had phlebograms made of the venous system. That was thought to be quite important at one time in this hospital. It is rarely, if ever, thought necessary now.

DR. BENJAMIN CASTLEMAN: It was done in 1943.

DR. ALLEN: Another point is that she had an operation devised by Dr. Linton several years ago of interruption of the communicating veins between the superficial and deep systems. This was preceded by a lumbar sympathectomy, probably done because she was said to have some difficulty with her arterial circulation as well, since it is recorded that no pulsations in the arteries were felt below the femoral veins. This operation of interruption of communicating veins between the superficial and deep systems has been fairly well abandoned now for a better procedure, which consists of stripping out the superficial system, the long saphenous and short saphenous veins if necessary, and interruption of the superficial femoral vein just below the profunda. These procedures are more apt to succeed in preventing recurrent illnesses from the lymphedema and ulceration that is so common as an aftermath of deep thrombophlebitis.

There is nothing much to say about some of these previous admissions other than what I have brought out, except that I should emphasize that we have done in this hospital very few interruptions of the vena cava. We have felt that many of the patients that might be subjected to this form of treatment actually do better with a procedure of less magnitude, that is, bilateral interruption of the femoral veins with removal of the thrombi, if present, and treatment with anticoagulants afterward. I think somewhere in the neighborhood of fifteen vena cava interruptions only have been done here during the time when we have had approximately 3000 patients under treatment, either prophylactically or therapeutically, for thrombophlebitis and pulmonary embolism. Interruption of the vena cava should be reserved, we believe, for those patients who are having septic infarcts arising from the pelvic veins. It is wise to interrupt also the ovarian or spermatic vein, as the case may be, provided these veins are also thrombosed. Although vena-cava interruption is a safe operation so far as life and death are concerned, it leaves these patients, as a rule, more handicapped than some of the less radical procedures that we have used.

Coming down to the final admission, the fifth admission, which is the present illness, it would be a natural supposition that the abdominal discomfort that this patient had might in some way be associated with her great tendency to thrombose her blood vessels. It is interesting that the pro-

thrombin level at the time of the second admission was 27 seconds, with a normal of 22 seconds, and on the last admission it was still a little higher than normal, 18 seconds. It is a fairly well understood fact throughout the country that we do not often have thrombophlebitis or thrombosis of blood vessels occur in persons who have a higher than normal prothrombin time. In the original studies of Bancroft et al.* on postoperative thrombophlebitis, all the patients who developed this complication had a lower than normal prothrombin time in the series of patients studied by him and his co-workers. We have plenty of cases here of patients who have had infarcts following treatment by anticoagulants with a prothrombin level above normal, although it is not common and we do not expect it.

The character of this woman's pain is interesting, and the onset is described as being fairly sharp and fairly sudden, but it does not give the impression of the onset of mesenteric thrombosis. There are at least two types of thrombosis with which I am familiar: thrombosis of the mesenteric artery and thrombosis of the venous system, which produce very different pictures. When the mesenteric thrombosis involves the arterial system, the pain is more excruciating than it is in almost any other disease. These patients are precipitated into shock from this pain. They have a weak pulse, and are gray, restless and sweating, and most patients who develop that difficulty are in the arteriosclerotic age group, and they are in a pretty hopeless state usually when they enter the hospital. In this type of thrombosis of the mesenteric vessels one almost invariably finds a high white-cell count. That is one of the helpful differential diagnostic points. It is not at all uncommon to find a count well into the forty thousands. Also this condition is progressive, although one may rarely find a favorable situation and a satisfactory outcome following resection of the involved small intestine. The mortality in this disease is extremely high.

In venous thrombosis, however, the onset is a little more insidious and is apt not to give as high a white-cell count, but even in that situation the patient should not be completely afebrile and in as good condition as this patient apparently was. It is possible for a venous thrombosis of the mesentery to carry on over a period of days as this patient did prior to the time that operation seemed indicated. I am inclined to think, having tried my best to pin this on some thrombotic mechanism of the vascular system within the abdomen, that perhaps it was not present in this case — that this woman had something else to account for her symptoms.

The commonest cause of epigastric distress, followed by nausea and vomiting, and pain settling in the right lower quadrant, is acute appendicitis. There are some features of the story that make one wonder if that was not really the cause of this disturbance. She had the proper white-cell count, the proper ratio of polymorphonuclear cells, and the only out about it, which might not be an out at all, is the apparent relief of pain on the third hospital day, with a recurrence twenty-four hours later. The fact that she was afebrile and had a normal pulse and so forth is somewhat in favor of some other very mild inflammatory affair or some mechanical effect. The reason I was interested in these shadows — you may not see them but they are present in the first films — is that I thought they could be in the course of the ureter. It is not too uncommon to have a Dietl's crisis mimic other situations in the abdomen. We recently had a patient sent into the hospital with what appeared to be full-blown acute intestinal obstruction. A plain film of the abdomen, instead of showing dilated gas-filled loops of bowel as suspected, showed a great many stones in the right kidney pelvis, with one or two down the course of the ureter. The urologist helped us out and passed the catheter up the patient's ureter and dislodged the stones and the symptoms of intestinal obstruction were immediately relieved. So it is possible that this woman under discussion could have had a ureteral stone.

Our attention is called to this spot in the ileum that looks atypical. We are carefully told in the history that this is not intestinal obstruction from the character of the peristaltic sounds heard through the stethoscope. I will be surprised if it turned out to be the site of this patient's difficulty, since I would not expect to find barium passing through the area so readily; also I believe the symptomatology would be different. It is obvious that the woman did not have intussusception. Intussusception of the small bowel is common enough, but it gives perfectly typical symptoms of small-bowel obstruction, which I am sure this woman did not have. Because an operation was performed — and I do not know whether anyone would consider cystoscopy an operation or not — I suppose that this

*Bancroft, F. W., Kugelmass, I. N., and Stanley-Brown, M. Evaluation of blood clotting factors in surgical diseases. *Ann. Surg.* 90:161-189, 1929.

woman had a laparotomy, and my opinion is that acute appendicitis was probably the reason for the exploration.

DR. ALFRED KRANES: Would the fact that the appendix was supposed to have been removed many years previously alter your opinion on that?

DR. ALLEN: Is it in the history? I read it and completely forgot it during my discussion of her interesting story.

DR. KRANES: The appendix may still be there.

DR. ALLEN: But probably not.

DR. CASTLEMAN: Why not make another choice?

DR. ALLEN: I will come back to ureteral colic as a second choice.

DR. CASTLEMAN: Dr. Hardy, will you tell us what Dr. Linton thought about this case?

DR. IRAD B. HARDY: To bring you up to date briefly about the previous operation, it is of interest that following vena-cava ligation she did, as Dr. Allen mentioned, have some disability in that prior to operation she had been quite a golfer and since the ligation she has never been able to make eighteen holes without fatigue. Also of interest, since interruption of the femoral veins, the legs have been well. That point did not seem clear in the record. She had no further ulcerations for some time, and it does not appear that she will. On admission to the hospital the idea was certainly in the back of Dr. Linton's mind that the process in the abdomen might be another manifestation of venous thrombosis since she had shown such a tendency to it. At about the time the gastrointestinal series was reported negative, it was realized that an intravenous pyelogram should precede everything and while planning that procedure, she began to get sicker and complained more of abdominal pain. Finally on the fifth or sixth hospital day it appeared necessary to explore her as an emergency without the benefit of getting her more adequately prepared in the way of antibiotics or a Miller–Abbott tube. However, a Levine tube was passed, and the patient was explored in the middle of the night.

CLINICAL DIAGNOSIS

Mesenteric venous thrombosis?

DR. ALLEN'S DIAGNOSIS

Ureteral stone.

ANATOMICAL DIAGNOSIS

Mesenteric venous thrombosis.

PATHOLOGICAL DISCUSSION

DR. HARDY: A loop of terminal ileum about a foot in length was found to be involved with venous mesenteric thrombosis, and the mesentery was involved over a great extent. In doing the resection to remove all the obviously involved mesentery, it became questionable whether the blood supply to the right colon had not become jeopardized, so that resection of the terminal ileum plus a right colectomy and an ileotransverse colostomy were performed. The patient did well for a few days after operation and then went into a peculiar state of peripheral vascular insufficiency with low blood pressure and cold and clammy upper extremities. The legs remained dry and fairly warm. The cause of the condition was uncertain. There was no evidence of intraperitoneal irritation. The heparin and penicillin she had been getting were omitted, and strangely enough her chart rapidly improved and she got out of the state of peripheral shock. The temperature, which had risen to 104°F., and the pulse came down. Since then she has rapidly improved and is doing very well now. We are considering the possibility of trying heparin-sensitivity tests on her but not too soon. The clotting time is being maintained at what we think is a satisfactory level. We were interested to know whether it was possible for heparin, which she was getting, to play a part in the postoperative picture. At the present time large maintenance doses of dicumarol are keeping the prothrombin time at a satisfactory level.

DR. CASTLEMAN: The specimen received showed an adherent thrombus in the ileocolic vein and most of its tributaries. There was infarction of all the terminal ileum, but microscopically the ascending colon was viable. The ordinary example of mesenteric venous thrombosis involves the larger veins, such as the superior mesenteric. The absence of involvement here of the larger veins might account for the minimal symptoms that she had before the final episode preoperatively. I believe this is the first case I have seen in which there was spontaneous thrombosis of a vein smaller than the superior or inferior mesenteric. I reviewed the sections of the femoral veins removed a couple of years ago, and they showed intimal sclerosis ; there was also a little intimal sclerosis in the ileocolic vein. I am still at a loss to explain this unusual condition.

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PHYSICIAN OF AYSGARTH

THE general practitioner, having suffered somewhat of an eclipse in the Age of Specialism, is returning to the favor that he merits. He has had special sections devoted to his calling in important medical associations, and an academy has been founded to which he may aspire. He has been the recipient of spontaneous tributes such as was accorded him by Miss Mary Ellen Chase in her address published in the *Journal* a month ago. Perhaps his next danger will be the risk of turning into that paradoxical paragon, the general specialist!

Miss Chase's tribute, however, was to a breed of physician somewhat more and somewhat less than the general practitioner. It was to the physicians who represent the essence of general practice — those rugged individualists, the country doctors. Of such basic fiber is Dr. William N. Pickles, of Aysgarth, Yorkshire, whose Cutter Lecture on Preventive Medicine appears in this issue of the *Journal*. Dr. Pickles also, in his life and his accomplishments, illustrates not so much the difference between the general practitioner and the specialist, as he does the advantages to be found in country practice over the limitations imposed by practice in the city.

This comparison is not a new one, and the idea is one to which many medical men take kindly, here as abroad. Physicians everywhere have been imbued with reverence for Withering and the Shropshire foxglove bells, and for Edward Jenner, who recorded the temperature of hibernating hedgehogs for John Hunter while mentally incubating his own great contribution to medicine. They remember with respect Crawford W. Long, of Georgia, and Ephraim McDowell, the backwoods ovariotomist, and a host of other country doctors whose services have been equally faithful if less eventful.

Dr. Pickles is a present example of one who has taken advantage of the peculiar opportunities afforded him as a country doctor to gather knowledge and to acquire wisdom and, by virtue of his intimate acquaintance with his people, to observe the character of disease and trace its spread through a familiarly known population.

Perhaps the secret of his success is best expressed by his own thoughts as he looked down upon his Yorkshire valley from an adjacent hilltop one summer evening:

> Our attractive little lake seemed to lie at my feet, and one by one I made out most of our gray villages with their pall of smoke. And as I watched the evening train creeping up the valley, with its pauses at our three stations, I had this strange thought, that there was hardly a man, woman or child in all those villages of whom I did not know even the Christian name and with whom I was not on terms of friendship.

A graduate of London University in 1910 and a member of the Royal College of Physicians of London, Dr. Pickles is a country practitioner and medical officer of health for the Aysgarth Rural District. He is the author of *Epidemiology in Country Practice*, published in 1939, and occupies the unique position for a rural health officer of being called

repeatedly in consultation by the principal health authorities in England and Scotland.

In 1935 he lectured on "Epidemiology in Country Practice" before the Royal Society of Medicine; he gave the Milroy Lecture before the Royal College of Physicians in 1942 and the Finlayson Lecture of the University of Glasgow in 1946. He studied the incubation period of epidemic hepatitis years before epidemic hepatitis acquired its current importance, and was the first to recognize the presence of Bornholm disease in Great Britain, and to describe its clinical and epidemiologic behavior.

He has developed to a high degree the pastoral qualities of the physician, at the same time making so fruitful a study of rural epidemiology that his influence has spread over the United Kingdom. What more can be said of anyone than that he tilled well the soil whereon he was placed?

BLUE SHIELD AND THE PREMATURE INFANT

ELSEWHERE in this issue of the *Journal* a Blue Shield release appears concerning the definition of obstetric services as they apply to the "routine" care of the premature infant. The point around which discussions may revolve is the statement that "during confinement of the mother, Blue Shield does not cover routine care rendered by other than the physician who accomplished the delivery." This statement implies that care of the premature infant may be a part of the routine care of the confinement and is not chargeable to Blue Shield as a legitimate added expense.

Criticism of the assumption that the care of a premature infant may in any case be routine has been the result, notably on the part of the *Norfolk Medical News*, which raises the question, in its issue of June 8, 1948, whether the care of the premature baby should ever be classified as other than a medical emergency. This classification was apparently so intended by the Massachusetts Department of Public Health when it sponsored Section 67A of Chapter 111 of the General Laws, providing for the reporting of the birth of a premature infant elsewhere than in a hospital and the transportation of such an infant to a hospital suitably equipped for its care.

The matter requires further clarification in order that the financial responsibility of Blue Shield may be fixed and criticism reduced to a minimum. Obviously an acceptable definition of prematurity should first be established, and weight is the simplest factor on which to base this classification. Five and a half pounds, or 2500 gm., has been used as such a standard, the incidence of births at this weight or less being from 5 to 6 per cent of the total. If 5 pounds is accepted as the standard the incidence is nearer 4 per cent. The group weighing from 5 to 5½ pounds and the group weighing less than 5 pounds at birth are approximately equal, with a very low mortality rate for the former. On this basis Massachusetts law defines prematurity as of 5 pounds or less and in New York, although 5½ pounds is accepted as the standard for prematurity, special care in premature centers is not offered unless the baby at birth weighs 4 pounds or less. The sound suggestion has been made that for Blue Shield purposes a birth weight of 4½ pounds or less be accepted as the criterion for prematurity.

Individual infants will vary greatly as to the amount of care required to start them safely on their way, but it should be accepted that the majority of premature infants as defined above will require special oversight and that only a very small minority, if any, should be considered as suitable candidates for the routine attention accorded the newborn. For practical purposes such care may be considered as part of the routine of an obstetric case only if it can be given safely by the physician who made the delivery, at the hospital where the delivery took place and then only during the period of confinement of the mother.

DIRECTOR-GENERAL OF WORLD HEALTH ORGANIZATION

DR. BROCK CHISHOLM, a Canadian, has been elected the first director-general of the World Health Organization, the *News Letter* of the Organization reports. Dr. Chisholm, born in Oakville, Canada, in 1897, entered the Canadian Army during World War I as a private, later receiving a commis-

sion. After the war he studied medicine, taking his degree at the University of Toronto. He served an internship in England, practiced general medicine in Canada and studied human relations at Yale, returning then to England to study psychiatry.

During the second World War he was appointed director-general of the Medical Services of the Canadian Army and helped to develop the Pulhems system for determining aptitudes. In November, 1944, he became Canada's first deputy minister of health in the newly organized Department of National Health and Welfare. Two years later he resigned this post to become executive secretary of the Interim Commission of the World Health Organization.

In 1945 Dr. Chisholm was cited in connection with the Albert A. and Mary Lasker Award for "safeguarding the mental health of Canadian soldiers as a psychiatrist, soldier, philosopher, and administrator."

Dr. Chisholm is to be congratulated on his election; our friends and neighbors across the border are to be congratulated on the selection of a native son for this eminent position.

POSTGRADUATE MEDICAL EDUCATION IN CONNECTICUT

EXPANSION of facilities for postgraduate medical education in Connecticut was recently announced by President Seymour of Yale University. In cooperation with the Connecticut State Medical Society, the University is inaugurating a program to provide for short and long refresher courses for Connecticut physicians and to assist small hospitals in training resident physicians who are preparing for various medical specialties. Dr. William R. Willard, associate professor of public health, has been named assistant dean in charge of postgraduate medical education.

The expanded program is an extension of already successful co-operation between the University and the State Society that has made possible year-round operation of an institute of occupational medicine and hygiene, a joint endeavor with various state mental hospitals on the part of the University and the Clinical Congress of the Society, held at Yale each fall, which attracts from 600 to 800 physicians to its sessions. Like the Postgraduate Lecture Course of the Massachusetts Medical Society, the Connecticut program offers physicians an opportunity to keep abreast of the latest advances in therapy and public health. Members of the medical profession in Connecticut and elsewhere will watch the development of the program with great interest.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CHANGE IN RATE FOR CRIPPLED-CHILDREN CARE

On or after October 1, the all-inclusive per diem rate paid by the Department of Public Health to hospitals for care of crippled children will be increased to $10.00. Until recently, when the Department of Public Health and the Department of Education were successful in increasing the amount, the rate paid had been $8.00.

In the past year in an attempt to set a standard rate for payments based upon actual cost to hospitals for services given, a study was made by the Department of Public Health in conjunction with the Departments of Welfare, Mental Health, Correction and Education and with the Industrial Accident Board. A plan, satisfactory to the hospitals rendering the services and to the Commonwealth as a purchasing agent, was drawn up by an unpaid commission composed of the heads of the departments previously mentioned with the co-operation of the Veterans Administration. The plan was incorporated in Senate Bill 430 (1948), and was presented before the recent legislature. However, this bill was not passed.

The defeat of the bill left the Department of Public Health in the position of paying for hospital services of certain programs at a rate not only below posted hospital charges but also below actual costs to the hospitals. In the care of crippled children and rheumatic-fever patients the department has been limited in reimbursements to all-inclusive per diem rates of $8.00. Reports from some hospitals of Greater Boston have shown that all-inclusive per diem cost for these patients approximates $16.00. The result is that certain hospitals are subsidizing crippled-children programs to the extent of $8.00 a day for each case.

The Department of Public Health hopes that this increase in rate will to some extent lighten the financial burden carried by the hospitals.

BLUE CROSS - BLUE SHIELD

OBSTETRIC COVERAGE

The Blue Shield subscriber certificate defines obstetric services in part as " . . . routine care of a full term or premature newborn, including circumcision, when undertaken during confinement of the mother and when provided by the physician who accomplished the delivery." In another section, routine care, including circumcision, of a full-term or premature newborn infant is excluded when undertaken during the confinement of the mother by any physician other than the one who accomplished its delivery. As applied to premature infants these provisions mean that:

During confinement of the mother, Blue Shield does not cover routine care rendered by other than the physician who accomplished the delivery.

After confinement of the mother, Blue Shield covers routine care rendered by any participating physician.

During and after confinement of the mother, Blue Shield covers other than routine care rendered by any participating physician.

Experience with these provisions has demonstrated that the question of whether there is such a thing as routine care of a premature infant is essentially academic because, even with the exclusion of coverage during confinement of the mother, most premature infants remain in the hospital in excess of the maximum number of benefit days provided by Blue Shield.

MISCELLANY

NEW FOUNDATION

The Arthritis and Rheumatism Foundation has been organized to promote a united nation-wide attack on arthritis and other rheumatic diseases, according to a release from W. Paul Holbrook, M.D., Tucson, Arizona, its president. The new Foundation is sponsored by the American Rheumatism Association in co-operation with the National Arthritis Research Foundation, The Detroit Fund for Crippling Diseases, and others.

"The organization," the release continues, "has been created to unite the efforts of lay and medical leaders in developing a new voluntary health agency, comparable, in the field of rheumatism, to such agencies as the National Tuberculosis Association, The National Foundation for Infantile Paralysis, and the American Cancer Society."

Its main objectives include the making of a nation-wide survey of what can and should be done to combat the problem of arthritis; arousing the public and the medical profession to the need for action in this field; and the financing of a program designed to accomplish those ends.

NOTICES

NORFOLK DISTRICT MEDICAL SOCIETY

The scientific meeting of the Norfolk District Medical Society will be held at 8 p.m. on Tuesday, September 28, at the Boston Medical Library, 8 Fenway, Boston, entitled "Specialty Night."

PROGRAM

The Relief of Common Eye Disorders Seen in General Practice. Dr. Edwin B. Dunphy.
The Relief of Common Ear, Nose and Throat Disorders Seen in General Practice. Dr. Leighton F. Johnson.
Dermatology in Relation to General Practice. Dr. Chester N. Frazier.

SOUTH BOSTON MEDICAL SOCIETY

The next meeting of the South Boston Medical Society will be held on Monday, October 4, at 9 p.m., in the auditorium of the Carney Hospital. The speaker will be Dr. Frank H. Lahey.

SUFFOLK DISTRICT MEDICAL SOCIETY

The fall dinner of Suffolk District Medical Society will be given at the Harvard Club of Boston on Saturday, October 9, at 7 p.m. The Honorable Christian A. Herter, United States Congress, will speak on "The Effect of Foreign Policy on Domestic Questions."

Members of the Massachusetts Medical Society, wives and friends are cordially invited.

UROLOGY AWARD

The American Urological Association offers an annual award of $1000 (first prize of $500, second prize $300 and third prize $200) for essays on the result of some clinical or laboratory research in urology. Competition is limited to urologists who have been in such specific practice for not more than five years and to residents in urology in recognized hospitals. All interested should write to the secretary, Dr. Thomas D. Moore, 899 Madison Avenue, Memphis, Tennessee. Essays must be in his hands before February 15, 1949. The first-prize essay will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Biltmore Hotel, Los Angeles, May 16 to 19.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, SEPTEMBER 23

FRIDAY, SEPTEMBER 24
*9:00 a.m.–12:00 m. Combined Medical and Surgical Staff Rounds. Peter Bent Brigham Hospital.

TUESDAY, SEPTEMBER 28
*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.
*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.
8:00 p.m. Norfolk District Medical Society. Boston Medical Library.

WEDNESDAY, SEPTEMBER 29
*12:00 m.–1:00 p.m. Clinical Conference. (Children's Hospital.) Amphitheater, Peter Bent Brigham Hospital.

*Open to the medical profession.

SEPTEMBER 18. College of American Pathologists. Page 418, issue of September 9.

SEPTEMBER 20–23. American Hospital Association. Page 310, issue of February 26.

SEPTEMBER 22. New England Conference of Industrial Physicians and Surgeons. Page 244, issue of August 5.

SEPTEMBER 28. Norfolk District Medical Society. Notice above.

SEPTEMBER 29. Mississippi Valley Medical Editors' Association. Page 170, issue of January 29.

OCTOBER 1 and 2. American Society of Anesthesiologists, Inc. Page 382, issue of September 2.

OCTOBER 1–MAY 20. Metropolitan State Hospital. Page 418, issue of September 9.

OCTOBER 4. South Boston Medical Society. Notice above.

OCTOBER 6–9. American Board of Ophthalmology. Page 170, issue of January 29.

OCTOBER 9. Suffolk District Medical Society. Notice above.

OCTOBER 14. The Practical and Clinical Sides of the Management of the Rh Problem in Pregnancy. Dr. William C. Moloney. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

OCTOBER 15. American Trudeau Society. Page 418, issue of September 9.

OCTOBER 18–22. American College of Surgeons. Page 417, issue of September 9.

OCTOBER 27. New England Obstetrical and Gynecological Society. Annual Meeting. Hotel Somerset, Boston.

NOVEMBER 1–3. American Clinical and Climatological Association. Page 582, issue of April 15.

NOVEMBER 3 and 4. Annual Meeting of National Committee for Mental Hygiene, Inc. Page 282, issue of August 12.

(*Notices concluded on page xvii*)